OIPE JC86 JUN 26 2003 PATENT & TRADEMARK OFFICE

RECEIVED #12 #10 7-2-03
JUL 01 2003
TECH CENTER 1600/2900

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

U.S. Serial No.:	10/076,937
Filing Date:	02/15/2002
Applicants:	Dean, Herbert M. et al.
Title:	DOSAGE UNIT FOR CARDIOPROTECTION
Atty. Docket No.:	dean0202con
Art Unit:	1617
Examiner:	Hui, San-ming R.

Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF DR. JERRY H. GURWITZ

I, Dr. Jerry H. Gurwitz, hereby declare the following:

1. I am Professor of Medicine, University of Massachusetts Medical School, Executive Director, Meyers Primary Care Institute, the Dr. John Meyers Chair in Primary Care Medicine at the University of Massachusetts Medical School, a Lecturer on Ambulatory Care and Prevention, Harvard Medical School, Chief of the Section for Health Services Research, Division of General Medicine and Primary Care, UMASS-Memorial Healthcare, Staff Physician at Saint Vincent Hospital, and Primary Care Physician, Fallon Clinic, Inc.

2. I have been practicing medicine since 1983 and have specialized in the treatment of the elderly with major research interests in adverse drug events, drug prescribing and utilization patterns, and clinical decision-making in the elderly patient population.

3. I have been a speaker at numerous professional meetings, conventions, institutes, forums, and medical schools. I am a co-author on many medical papers including papers relating to under-utilization of beta-blocker therapy in acute myocardial infarction, use of beta-blocker therapy after acute myocardial infarction, noncompliance with congestive heart failure therapy in the elderly, and the use of aspirin, beta-blockers and lipid lowering medications before recurrent acute myocardial infarction. My curriculum vitae is attached (Exhibit A).

4. Medical care ultimately costs less if successful interventions are done.

5. Numerous studies have shown the benefit of using beta-blockers, of using aspirin and of using lipid-lowering agents in patients who have had heart attacks, anginal symptoms, or are at high risk.

6. In my practice, I typically see elderly patients, many with a history of heart conditions.

7. Individuals with cardiovascular disorders are known to commonly utilize many medications. Older individuals are in the typical age group in which these cardio-preventative medications are required. Older patients are more susceptible to confusing their multiple medications and multiple treatment regimens.

8. Despite the industry's many years of knowledge of the benefits of using beta-blockers, of using platelet inhibitors such as aspirin and of using lipid-lowering agents in patients with established cardiac disease, and of the knowledge of compliance problems related to long-term treatments with multiple medications especially in older patients, the general approach is to educate physicians and patients.

9. Despite my intimate knowledge of adverse drug events, drug prescribing and utilization patterns, and clinical decision-making in the elderly patient population and despite the appreciably higher mortality rates associated with a recurrent acute myocardial infarction than that associated with a first acute myocardial infarction in the United States each year, I have not considered and never personally considered, nor has it ever occurred to me to combine beta-blockers and lipid-lowering agents into a single dosage unit as described in the above-captioned application.

10. The single-dose, beta-blocker and lipid-lowering agent described in the above-captioned application appears to be novel.

Declarant further states that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledg that willful false statements and the like so made are punishable by fine or imprisonment, or both, under

S ction 1001 of Titl 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 5/29/03 Name: Jerry H. Gurwitz, M.D.

OIPE JC86
JUN 26 2003
PATENT & TRADEMARK OFFICE

CURRICULUM VITAE

Date Prepared: January 15, 2003

Name: JERRY HOWARD GURWITZ

Address: 33 Metcalf Street, Worcester, MA 01609

Date of Birth: July 11, 1956

Place of Birth: Montgomery, Alabama

Education:

1978 A.B.	Dartmouth College
1983 M.D.	University of Massachusetts Medical School

Postdoctoral Training:

Internships and Residencies:

1983-84	Intern in Medicine, University of Massachusetts Hospital
1984-86	Medical Resident, University of Massachusetts Hospital

Fellowship:

1986-88	Clinical Fellow in Medicine, Division on Aging, Harvard Medical School
1986-88	Faculty Development Program, Division of General Medicine, Harvard Medical School
1986-89	Clinical Fellow in Medicine, Brigham and Women's Hospital
1988-89	Research Fellow in Medicine, Beth Israel Hospital

Licensure and Certification:

1985	Commonwealth of Massachusetts
1986	Diplomate, American Board of Internal Medicine
1988	Diplomate in Geriatric Medicine, American Board of Internal Medicine

Academic Appointments:

1988-1993	Instructor in Medicine, Harvard Medical School
1993-1996	Assistant Professor of Medicine, Harvard Medical School
1996-	Lecturer on Ambulatory Care and Prevention, Harvard Medical School
1996-	Associate Professor of Medicine, University of Massachusetts Medical School
1996-	The Dr. John Meyers Chair in Primary Care Medicine, University of Massachusetts Medical School
1999	Professor of Medicine, University of Massachusetts Medical School

Hospital/Clinical Appointments:

1988-1993	Geriatrician, Hebrew Rehabilitation Center for Aged, Boston
1988-1996	Attending Physician, Brockton/West Roxbury Veterans Administration Medical Center
1989-1996	Associate in Medicine, Beth Israel Hospital, Boston
1989-1996	Associate Physician, Brigham and Women's Hospital
1993-1996	Chief of Geriatric Medicine, Department of Medicine, Brockton Division, Brockton/West Roxbury Veterans Administration Medical Center
1996-	Chief, Section for Health Services Research, Division of General Medicine and Primary Care, UMASS-Memorial Healthcare
1996-	Staff Physician, Saint Vincent Hospital
1996-	Primary Care Physician, Fallon Clinic, Inc.

Other Professional Positions:

1990-1996	Assistant Director, Harvard Geriatric Education Center
1996-	Executive Director, The Meyers Primary Care Institute
1997-	Associate Director for Managed Care, Harvard Upper New England Geriatric Education Center

Awards and Honors:

1987-88	Charles A. Dana Foundation Fellow
1988-91	Merck Foundation Fellow in Geriatric Clinical Pharmacology
1991-96	Clinical Investigator Award, National Institute on Aging
1994	Fellow of the American College of Physicians
1994	Fellow of the American Geriatrics Society
1994	Fellow of the Gerontological Society of America
1996	Leon I. Goldberg Young Investigator Award, American Society for Clinical Pharmacology and Therapeutics

1996	Research Poster Award (Epidemiology), "Atrial Fibrillation in the Long-Term Care Setting," 1996 Annual Meeting of the American Geriatrics Society
1996	NESTOR Visiting Professor of Geriatric Medicine, The Netherlands Programme for Research on Aging
1996	Department of Veterans Affairs Certificate of Appreciation
1996	The Dr. John Meyers Chair in Primary Care Medicine, University of Massachusetts Medical School
1997	First International Visiting Scientist, Baycrest Centre for Geriatric Care, Ontario
1998	Outstanding Primary Care Researcher, University of Massachusetts Medical School Generalist Physician Initiative
1999	The Best of *Archives of Internal Medicine* 1999 *Arch Intern Med* 1999;159:561-7.
2000	Society of General Internal Medicine Initial Research Mentorship Award with Sumit Majumdar, MD
2001	William B. Abrams Award in Geriatric Clinical Pharmacology, American Society for Clinical Pharmacology and Therapeutics
2002	Alpha Omega Alpha Honor Medical Society, University of Massachusetts Medical School, Alumnus Member

Major Committee Assignments:

National and Regional:

1994	Committee member, Massachusetts Governor's Conference on Alzheimer's Disease
1995-2005	Expert Advisory Panel on Gerontology, The United States Pharmacopeial Convention (USP)
1996-	National Scientific Advisory Council, American Federation for Aging Research
1996	Oversight Committee for NIH-funded study: "Physical Activity Promotion for CHD Risk Reduction," Harvard Pilgrim Health Care
1996	Grant reviewer, The Physicians' Services Incorporated Foundation, Ontario, Canada
1996	Expert Advisory Panel on Geriatrics, The United States Pharmacopeial Convention (USP) Subcommittee on Botanicals
1996	Reviewer, Institute of Medicine Report: "Health Outcomes for Older People: Questions for the Coming Decade"
1996	Medication Error Reduction Initiative Coalition Member, American Medical Association
1996	Governing Board, The HMO Research Network

1997	Physician Prescribing Practices Expert Panel, Institute for Healthcare Improvement
1997- 2000	Representative of the American Geriatrics Society to the United States Pharmacopeial Convention (USP)
1997	American Heart Association Project on Guidelines for Uniform Reporting of Risk Reduction Outcomes - Section on Beta Blockers Post MI
1997-2001	Agency for Health Care Policy and Research Study Section Member Health Care Quality and Effectiveness Research
1997-1998	Prescribing Practices Collaborative, Institute for Healthcare Improvement, Advisory Group
1998	Reviewer for Robert Wood Johnson Changes in Health Care Financing and Organization Initiative
1999	SCRIPT Technical Expert Panel, Coalition for Quality in Medication Use
1999	American Society for Consultant Pharmacists, Technical Advisory Group, Fleetwood Project
1999	American Federation for Aging Research, Merck/AFAR Scholarship Program in Geriatric Clinical Pharmacology Awards Selection Committee
1999	National Health Care Quality Improvement Program (HCQIP) Initiative to Improve Quality of Care for Atrial Fibrillation Expert Panel
1999	Safety Monitoring Board for NIH-funded study "Aging, Hypertensive Therapy, and Blood Pressure Regulation"
1999	National Heart, Lung, and Blood Institute, Working Group on Adherence to Medical and Lifestyle Interventions
2000	Chair, Scientific Abstract Review Subcommittee, Provider/Organization-Centered Research, Society of General Internal Medicine, 23rd Annual Meeting
2000	American Society for Consultant Pharmacists Foundation, "Pharmacist-Sensitive Outcomes" Advisory Board
2000	Guest Expert Advisor on Risk Management, FDA Division of Gastrointestinal and Coagulation Drug Products (alosetron)
2000-2005	Representative of the American Geriatrics Society to the United States Pharmacopeia (USP) Convention
2002	Massachusetts Department of Public Health Advisory Panel on Experimental/Investigational Medical and Surgical Procedures
2002	National Committee for Quality Assurance (NCQA) Medication Management Technical Subgroup

University of Massachusetts Medical School:

1996-2000	University of Massachusetts Medical School Admissions Committee

1996-	University of Massachusetts Medical School, Robert Wood Johnson Generalist Physician Initiative Directors' Group
1997	CME Advisory Committee Task Force, University of Massachusetts Medical Center, Managed Care Strategies and Physician Retraining
1998	Member, Search Committee, Department of Medicine Chair
1999	Chancellor's Task Force on Clinical and Population-based Research at University of Massachusetts Medical School
1999	Ad Hoc Search Committee for Outcomes Researcher, Department of Pediatrics
2000	Advisory Committee for the University of Massachusetts Medical School Macy Initiative in Health Communication
2000	Member, Search Committee, Department of Medicine Vice Chair for Research
2001	University of Massachusetts Medical School Clinical Research Advisory Committee
2002	University of Massachusetts Medical School/AAMC/Hartford Foundation Geriatrics Project – Consultant

Hospital:

Brigham and Women's Hospital

1993-1996 Medication Education and Management Committee

Brockton/West Roxbury Veterans Affairs Medical Center

1994-1995 Inpatient Consolidation Committee

Beth Israel Hospital

1988-1994 Transfusion Committee
1989-1992 Pharmacy and Therapeutics Committee
1990-1992 Therapeutic Drug Monitoring Committee

Hebrew Rehabilitation Center for Aged:

1987-1993	Pharmacy and Therapeutics Committee (Chairman)
1988-1993	Patient Care Assessment Committee
1988-1993	Utilization Review Committee
1990-1993	Transfusion Committee (Chairman)

Fallon Healthcare System

1996-	Advisory Team for Senior Health
1998-	Fallon Elder Service Plan Medical Advisory Committee
1999-	Institutional Review Board, Fallon Healthcare System and Saint Vincent Hospital
1999-	Technology Assessment Committee, Fallon Community Health Plan

Memberships, Offices and Committee Assignments in Professional Societies:

1985-	American Geriatrics Society
1988-	Gerontological Society of America
1989-1994	American Society for Clinical Pharmacology and Therapeutics Vice Chairperson, Section on Geriatric Clinical Pharmacology
1991-	American College of Physicians
1994-1997	American Society for Clinical Pharmacology and Therapeutics Chairperson, Section on Geriatric Clinical Pharmacology
1994-1997	Committee on Coordination of Scientific Sections, American Society for Clinical Pharmacology and Therapeutics
1995-1997	Board of Directors, American Society for Clinical Pharmacology and Therapeutics
1995-	International Society for Pharmacoepidemiology
1996-	Association for Health Services Research
1996-	Society of General Internal Medicine
1996-1997	Nominating Committee, American Society for Clinical Pharmacology and Therapeutics

Editorial Boards:

1992	Editorial Advisory Board, *AARP Prescription Drug Handbook*
1994-1999	Editorial Board, *Journal of the American Geriatrics Society*
1995	Deputy Editor, *Journal of Gerontology: MEDICAL SCIENCES*
1995-1999	Editorial Board, *Journal of Gerontology: MEDICAL SCIENCES*

Major Research Interests:

1. Adverse drug events
2. Drug prescribing and utilization patterns
3. Clinical decision-making in the elderly patient population

Research Funding Information:

Past:

1988-1991 American Federation for Aging Research PI
NSAID-Associated Azotemia in the Elderly

1989-1991 Ocean Spray Cranberries, Inc. Co-investigator
Prevention of Urinary Tract Infections in the Elderly

1990-1991 NIH/Harvard GRTC (Pilot Project Grant) PI
Thiazide Diuretic Therapy and Initiation of Treatment for Diabetes Mellitus

1991-1992 Geriatric Drug Therapy Institute PI
Constipation and Laxative Use in the Institutionalized Elderly

1991-1992 NIH/RO1 Co-investigator
Drug-Induced Parkinsonian Symptoms in the Elderly

1992-1993 Kabi Pharmacia Co-investigator
The Cost-Effectiveness of Thrombolytic Therapy

1992-1993 The Medical Foundation/Charles H. Farnsworth TrustPI
Compliance with Glaucoma Therapy in the Elderly

1994-1995 Dupont Pharma PI
Clinical Decision-Making in the Use of Anticoagulant Therapy in Elderly Patients with Atrial Fibrillation

1991-1996 NIH/KO8 PI
Drug-Induced Illness in the Elderly: NSAIDs as a Model

1992-1996 NIH/RO1 Co-investigator
Improving Quality of Breast Cancer Care in Elderly Women

1992-1996 NIH/RO1 Co-investigator
Improving Compliance with Acute MI Practice Guidelines

1996-1998 NIH/RO1 PI
Prevention of Adverse Drug Events in the Nursing Home Setting

1996-1998 NIH/RO1 Co-PI
Risky Geriatric Benzodiazepine Use: Predictors and Trends

1996-1998 NIH/RO1 Co-investigator
Medicare Capitation and Quality of Care for Acute MI

1996-1998 Dupont Pharma PI
Improving the Quality of Anticoagulation Care in the Long-Term Care Setting

1997-2000 Health Resources and Services Administration PI
Geriatric Education Centers Training Program
(subcontract with Harvard Division on Aging)

1997-1998 Healey Endowment Fund PI
Medical Educators in the Managed Care Setting

1997-1998 Merck, Inc. PI *Epidemiologic Study of Gastric and Duodenal Safety in Patients on Alendronate (subcontract with Harvard Pilgrim Health Care)*

1998-2000 Robert Wood Johnson Foundation Co-investigator
Impact of Physician Compensation Mechanisms on the Process of Care

1998-1999 Solvay Pharmaceuticals, Inc. PI
Comprehensive Evaluation of a Premarin-to-Estratab Switch in a Managed Care Setting

1998-2000 Partnership for Quality Education Co-PI
Managed Care of the Elderly

1998-1999 American Society of Consultant Pharmacists PI
Research and Education Foundation
Drug Benefit Plans for the Elderly under Managed Care

Current

1996-2000 NIH/RO1 Co-investigator
Adjuvant Tamoxifen Therapy in Old Age

1998-2002 National Cancer Institute Co-Investigator
HMO Research Network/Cancer Research Network

1997-2002	Food and Drug Administration *Consequences of Outpatient and Inpatient Drug Exposures* (Subcontract with Harvard Pilgrim Health Care)	PI
1998-2000	National Institute on Aging *Adverse Drug Events in the Ambulatory Geriatric Setting*	PI
2000-2003	Agency for Healthcare Research and Quality *Reduction of Adverse Drug Events in the Nursing Home*	PI
2000-2003	Agency for Healthcare Research and Policy *Centers for Education and Research on Therapeutics*	Co-Investigator
2000-2004	National Cancer Institute *Breast Cancer Treatment Outcomes in Older Women*	Co-Investigator
2000-2004	Health Resources and Services Administration *Geriatric Education Centers Training Programs*	Co-Investigator
2000-2003	Health Resources and Services Administration *Academic Administrative Units in Primary Care*	PI

Principal Clinical and Hospital Services Responsibilities:

1988-1993	Staff Geriatrician, Hebrew Rehabilitation Center for Aged, Roslindale, MA
1989-1991	Attending Physician, Geriatric Consultation Service, Beth Israel Hospital, Boston, MA
1988-1996	Attending Physician, Geriatric Evaluation and Management Unit, West Roxbury Veterans Administration Medical Center, West Roxbury, MA
1989-1996	Attending Physician, Geriatric Outpatient Clinic, Brigham and Women's Hospital
1990-1996	Attending Physician, Medical Service, Brockton/West Roxbury Veterans Administration Medical Center, West Roxbury, MA
1992-1996	Attending Physician, Geriatric Consultation Service, Brigham and Women's Hospital
1993-1996	Attending Physician, Geriatrics and Extended Care Service, Brockton Division, Brockton/West Roxbury VAMC
1994-1996	Attending Physician, Medical Service, Brigham and Women's Hospital

1996- Teaching Attending Physician, University of Massachusetts Medical Center

Major Administrative Responsibilities:

1990-1996 Assistant Director, Harvard Geriatric Education Center
1993-1996 Chief of Geriatric Medicine, Department of Medicine, Brockton Division, Brockton/West Roxbury Veterans Administration Medical Center
1996- Executive Director, The Meyers Primary Care Institute
1996- Section Chief, Section for Health Services Research, Department of Medicine, Division of General Medicine, Primary Care, and Geriatrics, University of Massachusetts Medical School

Self report of teaching:

Local Contributions:

Harvard University: Harvard Medical School and Harvard School of Public Health

1988-1996 Introduction to Clinical Medicine
Introduction to Geriatrics and Long-Term Care
4-10 students
3 hours/year

1991 Department of Continuing Education
Primary Care Internal Medicine: Principles and Practices
Lecturer on Geriatric Clinical Pharmacology

1989-1992 Department of Continuing Education
Geriatric Medicine Course
Lecturer and Workshop Leader on Geriatric Clinical Pharmacology

1992-1993 Department of Continuing Education
New Pathways in General Medical Education
Workshop Leader

1991-1996 Pharmacology Module (New Pathway)
Tutorial Leader
9-10 students
4 weeks/year (25-30 hours)

1994-1996 Pain: Exploring Issues from Sensory Receptors to Societal Concerns (ABS Elective SM 512.0)
5-6 students
2 hours/year as Lecturer

1997, 1998, 1999, 2001 Harvard School of Public Health Summer Epidemiology Program
5 fellows
2 hours as Workshop Leader

Beth Israel Hospital

1989-1991 Geriatric Medicine Consultation Service
Consult Attending
1 geriatric medicine fellow
1 month/year

1988-1996 Gerontology Division Seminars
Presenter
1-2 hours/year

1992 Department of Anesthesia and Critical Care
Grand Rounds
"Pharmacological Issues for the Elderly"

Hebrew Rehabilitation Center for Aged

1988-1993 Long-Term Care Clinical Rotation
Attending
1 geriatric medicine fellow; 0-1 residents; 0-1 medical students
3-4 months/year

Brockton/West Roxbury VAMC

1988-1996 Geriatric Evaluation and Management Unit Clinical Rotation
Attending
1 geriatric medicine fellow; 1 medical resident
1 month/year

1990-1996 Medical Service
Attending

1 resident; 2 interns; 2 medical students
1 month/year

1993-1996 Medical Resident Noon Conference Series
Presenter
4-5 hours/year

Brigham and Women's Hospital

1989-1996 Geriatric Outpatient Evaluation Clinic
Attending
1 geriatric medicine fellow
2 afternoons/month

1992-1996 Geriatric Medicine Consultation Service
Attending
1 geriatric medicine fellow
1 month/year

1994-1996 Medical Service
Attending
1 resident; 2 interns; 1-2 medical students; 2 pharmacy interns
1 month/year

1995-1996 Brigham Internal Medicine Associates Residents' Practice
Geriatric Medicine Attending
4-5 interns and residents
12 hours/year

University of Massachusetts Medical School

1996- Evidence Based Medicine Workshop (Department of Family Practice)
Critical Appraisal of Articles Related to Diagnosis
50 residents
3 hours

1997- Lecturer, Nurse Practitioner Pharmacology Course
11 students
2 hours

1997-2001 Medical Service
Teaching Attending

1 resident; 2 interns; 1 medical student
1 month

2001, 2002 Instructor, Introduction to Grant Writing Course,
University of Massachusetts Medical School
Department of Faculty Administration

2001 Interclerkship on Geriatric Medicine for 3rd Year Students
Lecturer
20 students

2002 Geriatrics Miniselective for 4th Year Students
Lecturer
5 students

Saint Vincent Hospital/
Worcester Medical Center

2002 Medical Service
Teaching Attending
1 resident, 1 intern, 1 medical student
1 month

Leadership Roles

1997-2002 Interclerkship on Managed Care for 3rd year students
Course Co-Director
115 medical students
16 hours

1997-2001 Practicing and Teaching Evidence-Based Medicine
(Sponsored by RWJ Generalist Physician Initiative)
Course Co-Director
16 community-based UMMS faculty
6 hours

1996-2002 Residency Curriculum on Managed Care
(Sponsored by RWJ Generalist Physician Initiative)

2002 Practicing and Teaching Evidence-Based Medicine
(Sponsored by RWJ Generalist Physician Initiative)
Course Co-Director
24 residents and fellows

Preparation of Teaching Materials/Curriculum Development

1992 Cardiovascular Pharmacology Case Study- New Pathway
Principles of Pharmacology Course (Harvard Medical School - 1)
"A Broken Heart"

1993 "H2 Blockers: Too Much of a Good Thing?"
Brigham and Women's Hospital
Medication Education and Management Program

Selected Regional, National, and International Contributions:

Invited Presentations

1990 Symposium Speaker, "Old age - is it a risk factor for adverse drug reactions?" IVth World Conference on Clinical Pharmacology and Therapeutics, Heidelberg, Germany

1990 Speaker, Geriatrics Board Review Course, American Geriatrics Society and the American College of Physicians, New Orleans, Louisiana, "Principles of Geriatric Pharmacology," "Nursing Home Pharmacology," "Iatrogenesis"

1990 Symposium Speaker, "Unique Aspects of Prescribing for the Elderly," Office of the Inspector General, Office of Evaluation and Inspections, Washington, D.C.

1991 Panelist, Research Priorities for Studying the OBRA Drug Regulations, Health Care Financing Administration, Washington, D.C.

1991 Speaker, American College of Physicians Annual Meeting, New Orleans, Louisiana, "Pharmacoepidemiology- Understanding and Using Epidemiological Data to Advance Therapeutic Skills"

1992 Symposium Speaker, "Explaining the risks of nonsteroidal anti-inflammatory drug therapy in the elderly: pharmacokinetics, pharmacodynamics, aging physiology, or comorbidity?" Vth World Conference on Clinical Pharmacology and Therapeutics, Yokohama, Japan.

1992 Testimony to the House Small Business Subcommittee on Regulation, Business Opportunities, and Energy, "Drug Product Labeling and the Appropriate Use of Prescription and OTC Drugs in the Elderly," Washington, D.C. (April 28, 1992)

1992 Speaker, "Food and Drug Administration Guideline for the Study of Drugs in Elderly Patients," American College of Cardiology Workshop- Inclusion of Elderly Individuals in Clinical Trials: Cardiovascular Disease and Cardiovascular Therapy as a Model, Bethesda, Maryland.

1992 Continuing Medical Education Course Speaker, "Drug Therapy in the Elderly," American Geriatrics Society and the American College of Physicians, San Francisco, CA

1992 Seminar Speaker, Brown University Center for Gerontology and Health Care Research, "Clinical, Epidemiologic, and Policy Issues Regarding Medication Use in the Long-Term Care Setting"

1994 Speaker, Boston City Hospital Primary Care Training Program Lecture Series, "Prescribing to the Elderly"

1994 Speaker, Veterans Administration National Training Program- Medication Management in the Elderly, "NSAIDs: A Model for Studying Drug Risk in the Elderly"

1994 Speaker, Temple University School of Medicine Geriatric Board Review Course, "Principles of Pharmacology in the Elderly"

1994 Speaker, Clinical Pharmacology Division, Indiana University School of Medicine, "Issues in Geriatric Clinical Pharmacology"

1994 Panelist, National Institute on Aging/National Cancer Institute/Agency for Health Care Policy and Research Working Group on Pharmacology in Aging and Cancer

1995 Meet the Professor, 1995 Annual Meeting of the American Geriatrics Society, "Geriatric Clinical Pharmacology"

1995 Medical Grand Rounds, University of Massachusetts Medical Center, "Optimal Drug Therapy in the Elderly"

1995 Medical Grand Rounds, Dartmouth-Hitchcock Medical Center, "Geriatric Clinical Pharmacology for Internists"

1995 Seminar Speaker, Department of Health Care Policy, Harvard Medical School, "A Very Large Acute Myocardial Infarction Database: Strengths and Weaknesses of Large Numbers"

1996 Invited Speaker, "Reduction of Bacteriuria and Pyuria following Ingestion of Cranberry Juice" 1996 Annual Meeting of the International Life Sciences Institute, Cancun, Mexico.

1996 Pharmacoepidemiology Seminary Series, Harvard School of Public Health, Department of Epidemiology, "Clinical Decision-Making in the Use of Warfarin in the Frail Elderly"

1996 NESTOR Visiting Professor of Geriatric Medicine, The Netherlands Programme for Research on Aging, "Introduction to Geriatric Clinical Pharmacology," University Hospital Nijmegen, Nijmegen, The Netherlands

1996 Invited Speaker, "Trends in Thrombolytic Use in the Elderly: Findings from the National Registry of Myocardial Infarction," Annual Drug Information Association Meeting on Statistical Issues in the Pharmaceutical Industry.

1996 Medical Grand Rounds, Brockton/West Roxbury VA Medical Center, "Clinical Decision-Making: Use of Warfarin in the Frail Elderly"

1996 Invited Speaker, "Drug Therapy in the Elderly", Successful Aging Course for visiting Japanese delegation, Harvard Geriatric Education Center

1996 Invited Speaker, "Polypharmacy in the Nursing Home", Massachusetts Extended Care Federation

1996 Pediatric Grand Rounds, University of Massachusetts Medical Center, "The Truth About Evidence-Based Medicine"

1996 Medical Grand Rounds, COLUMBIA Metrowest Medical Center, "Drug Therapy in the Elderly"

1996 Family Practice Grand Rounds, The Memorial Hospital, "Optimal Drug Therapy in the Elderly"

1996 Medical Grand Rounds, Champlain Valley Physicians Hospital Medical Center, Plattsburgh, NY, "Optimal Drug Therapy in the Elderly"

1997 Medical Grand Rounds, The Memorial Hospital, "Optimal Drug Therapy in the Elderly"

1997 Keynote Speaker, Health Care Financing Administration Office of Managed Care, Medications Quality Improvement Project Meeting

1997 Annual Meeting of the American Geriatrics Society and the American Federation for Aging Research, Symposium Speaker, "Is Oral Anticoagulation Risky? Evaluating the Reality."

1997 First Annual Symposium of University of Massachusetts Medical Center Heart Institute (Contemporary Strategies in the Treatment of Ischemic Heart Disease), Speaker, "Cardiac Care in an Aging Population"

1997 Annual Meeting of the Academy of Managed Care Pharmacy, Speaker, "Risk Management Issues in Pharmaceutical Care for the Elderly"

1997 Summer Institute on Aging Research sponsored by the National Institute on Aging, Lecturer, "Introduction to Geriatric Pharmacoepidemiology"

1997 University of Massachusetts Medical Center Second Annual Symposium on Thrombosis, Thrombolysis, and Anticoagulation for the Clinician, "Managing Anticoagulation in the Elderly"

1997 Boston University School of Medicine Epidemiology of Aging Course, Lecturer, "Pharmacoepidemiology in the Elderly"

1998 Boston University School of Medicine

Epidemiology of Aging Course, Lecturer,
"Pharmacoepidemiology in the Elderly"

1998 Elder Care 1998, Plenary Speaker, "Medication Issues in the Elderly," Worcester, MA

1998 Annual Meeting of the American Geriatrics Society, Update on Long-Term Care: "The Prescribing Cascade"

1998 Northeast Group on Educational Affairs 1998 Regional Meeting, "Teaching and Learning in the Era of Evidence-Based Medicine"

1998 Quality of Care Seminar Series, Harvard School of Public Health, "The Quality of Anticoagulation Care in the Frail Elderly"

1998 Drug Information Association Annual Meeting, Boston, MA, "An Update on Drugs in the Elderly – The Therapeutic Cascade"

1998 University of Massachusetts Third Annual Thrombosis, Thrombolysis and Anticoagulation for the Clinician Symposium; "The Safety and Efficacy of Anticoagulants in the Elderly"

1998 Boston University Center for Excellence in Geriatrics Boston, MA, "Polypharmacy"

1998 Harvard Division on Aging Grand Rounds, "Anticoagulation Care in the Elderly"

1998 Blue Cross Blue Shield Association Medicaid and Medicare Best Practices Forum, "Polypharmacy Management in Medicare Patients"

1999 Boston University School of Medicine
Epidemiology of Aging Course, Lecturer,
"Pharmacoepidemiology in the Elderly"

1999 Workshop, Mock Grants Review Study Section, Sponsored by the Agency for Health Care Policy and Research, HMO Research Network Meeting

1999 Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, "Strategies to Detect and Reduce Adverse Drug Events in the Nursing Home"

1999 Plenary Talk: "Considerations in Designing an 'Ideal' Medication Use System" at National Interdisciplinary Conference Sponsored by the Joint Commission of Pharmacy Practitioners – Re-Engineering the Medication Use System

1999 Harvard Medical School Department of Continuing Education – Topics in Long-Term Care, "Medication Use In the Nursing Home"

1999 Berkshire Medical Center Medical Grand Rounds, "Drug Prescribing in the Elderly"

1999 UMASS Memorial Health Care, Department of Medicine Grand Rounds, "Thrombolytic Therapy in the Elderly – A Dilemma in Therapeutic Decision-Making"

1999 Saint Vincent Hospital, Department of Medicine Grand Rounds, "Thrombolytic Therapy in the Elderly – A Dilemma In Therapeutic Decision-Making"

1999 National PACE Association Annual Conference, "Optimal Drug Therapy for the Elderly"

1999 University of Connecticut Center on Aging Geriatrics Grand Rounds, "Drug Therapy in the Elderly"

2000 Harvard Medical School Division on Aging Managed Care for the Elderly Conference, "Medication Issues"

2000 American Heart Association Scientific Conference on Existing Databases: Do they hold the answers to clinical questions in geriatric cardiovascular disease and stroke? "Acute Myocardial Infarction, Thrombolytic Therapy"

2000 Worcester Medical Center Grand Rounds, "To Err is Human: "Preventing Medication Errors and Adverse Drug Events in the Elderly"

2000 8th Annual Symposium on Geriatric Research and Health Care Policy, Hebrew Rehabilitation Center for Aged, "Making Drug Therapy Safer for the Elderly"

2000 Fifth Annual UMASS Thrombosis, Thrombolysis, and Anticoagulation for the Clinician Symposium, "Warfarin"

2000 Hospital of Saint Raphael, Medical Grand Rounds, "Optimal Drug Therapy in the Elderly"

2001 University of Massachusetts and UMASS Memorial Medical Grand Rounds, "To Err is Human, Making Medication Use Safer for the Elderly"

2001 Geriatric Educational National Retreat: Integrating Geriatrics into Neurology and Psychiatry, Sponsored by the American Geriatrics Society and the John A. Hartford Foundation, "Geriatric Clinical Pharmacology"

2001 Centers for Education and Research on Therapeutics, University of North Carolina, "Improving Communication of Drug Risk Information to Prevent Patient Injury"

2001 National Council on Patient Information and Education (NCPIE), 13th National Conference, Bethesda, MD "Promoting Safe Medication Use in Long-Term Care Settings"

2001 18th Annual Peter Lamy Conference – Building Bridges in Drug Therapy and Aging, University of Maryland School of Pharmacy, Keynote Speaker, "To Err is Human: Making Medication Use Safer for Elderly Patients"

2001 54th Annual Scientific Meeting of the Gerontological Society of America. Symposium Discussant: "Improving Medication Use in Home-Health and other Frail Community-Dwelling Elderly."

2002 Visiting Lecturer, Georgetown University Medical School, Clinical Pharmacology 45h Year Course, "Drug Therapy in the Elderly."

2002 Harvard Medical School Division on Aging Geriatric Grand Rounds, "Improving the Safety of Medication Use in the Elderly".

2002 Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics, "Special Populations and Pharmacotherapy"

2002 Institute of Medicine Workshop, "Role of Providers in the Clinical Research Enterprise"

Bibliography

Journals:

1. Gurwitz JH, Goldberg RJ, Holden A, Knapic N, Ansell J. Age-related risks of long-term oral anticoagulant therapy. Arch Intern Med 1988; 148:1733-6.

2. Goldberg RJ, Gore JM, Gurwitz JH, Alpert JS, Brady P, Strohsnitter W, Chen Z, Dalen JE. The impact of age on the incidence and prognosis of initial acute myocardial infarction: the Worcester Heart Attack Study. Am Heart J 1989; 117:543-9.

3. Gurwitz JH, Avorn J, Ross-Degnan D, Lipsitz LA. Nonsteroidal anti-inflammatory drug-associated azotemia in the very old. JAMA 1990; 264:471-75.

4. Gurwitz JH, Osganian V, Goldberg RJ, Chen Z, Gore JM, Alpert JS. Diagnostic testing in acute myocardial infarction: Does patient age influence utilization patterns? Am J Epidemiol 1991; 134:948-57.

5. Gurwitz J, Clive DM, Rossetti R, Stoff JS. The effects of nonsteroidal anti-inflammatory drugs on renal function in the healthy old. J Nephrol 1991; 3:163-167.

6. Clive DM, Gurwitz J, Rossetti R. The effects of nonsteroidal anti-inflammatory drug therapy on potassium homeostasis in healthy subjects. Am J Kidney Dis 1992; 19:16-21.

7. Gurwitz JH, Noonan JP, Sanchez M, Prather W. Barium enemas in the frail elderly. Am J Med 1992; 92:41-44.

8. Gurwitz JH, Noonan JP, Soumerai SB. Reducing the use of H2 receptor antagonists in the long-term care setting. J Am Geriatr Soc 1992; 40:359-364.

9. Gurwitz JH, Avorn J, Ross-Degnan D, Choodnovskiy I, Ansell J. Aging and the anticoagulant response to warfarin. Ann Intern Med 1992; 116:901-904.

10. Goldberg RJ, Gurwitz JH, Yarzebski J, Landon J, Gore JM, Alpert JS. Patient delay and receipt of thrombolytic therapy among patients with acute myocardial infarction: a community wide perspective. Am J Cardiol 1992; 70:421-425.

11. Gurwitz JH, Col NF, Avorn J. The exclusion of elderly and women from clinical trials in acute myocardial infarction. JAMA 1992; 268:1417-1422.

12. Gurwitz JH, Goldberg RJ, Chen Z, Gore JM, Alpert JS. Beta-blocker therapy in acute myocardial infarction: Evidence for underutilization in the elderly. Am J Med 1992; 93:605-610.

13. Pagley PR, Yarzebski J, Goldberg R, Chen Z, Chiriboga D, Dalen P, Gurwitz J, Alpert JS, Gore JM. Gender differences in the therapeutic management of patients with acute myocardial infarction: a multi-hospital, community-based perspective. Arch Intern Med 1993; 153:625-629.

14. Chiriboga DE, Yarzebski J, Goldberg RJ, Chen Z, Gurwitz J, Gore JM, Alpert JS, Dalen JE. A community-wide perspective of gender differences and temporal trends in the use of diagnostic and revascularization procedures for acute myocardial infarction: the Worcester Heart Attack Study. Am J Cardiol 1993; 71:268-273.

15. Gurwitz JH, Bohn RL, Glynn RJ, Monane M, Mogun H, Avorn J. Antihypertensive drug therapy and initiation of treatment for diabetes mellitus. Ann Intern Med 1993; 118:273-278.

16. Gurwitz JH, Glynn RJ, Monane M, Everitt DE, Gilden D, Smith N, Avorn J. Adherence to treatment for glaucoma among the elderly. Am J Public Health 1993; 83:711-716.

17. Gurwitz JH, Bohn RL, Glynn RJ, Monane M, Mogun H, Avorn J. Glucocorticoids and the risk for initiation of hypoglycemic therapy. Arch Intern Med 1994; 154:97-101.

18. Glynn RJ, Gurwitz JH, Bohn RL, Monane M, Avorn J. Old age and race as determinants of initiation of glaucoma therapy. American Journal of Epidemiology 1993; 138:395-406.

19. Avorn J, Glynn RJ, Gurwitz JH, Bohn R, Monane M, Gilden D, Everitt DE, Choodnovskiy I. Adverse pulmonary effects of topical beta-blockers used in the treatment of glaucoma. J Glaucoma 1993; 2:158-165.

20. Ross-Degnan D, Soumerai SB, Fortess EE, Gurwitz JH. Examining product risk in context: market withdrawal of zomepirac sodium as a case study. JAMA 1993; 270:1937-1942.

21. Rochon PA, Gurwitz JH, Simms RW, Fortin PR, Felson DT, Minaker KL, Chalmers TC. A study of manufacturer supported trials of nonsteroidal anti-inflammatory drugs: Reporting and documentation of efficacy and toxicity results. Arch Intern Med 1994; 154:157-163.

22. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Avorn J. Noncompliance with congestive heart failure therapy in the elderly. Arch Intern Med 1994; 154:433-437.

23. Col NF, Gurwitz JH, Alpert JS, Goldberg RJ. Frequency of inclusion of patients with cardiogenic shock in trials of thrombolytic therapy. Am J Cardiol 1994; 73:149-157.

24. Gurwitz JH, Sanchez-Cross MT, Eckler MA, Matulis J. The epidemiology of adverse and unexpected events in the long-term care setting. J Am Geriatr Soc 1994; 42:33-38.

25. Pickering T-D, Gurwitz JH, Zaleznik D, Noonan JP, Avorn J. The appropriateness of oral fluoroquinolone prescribing in the long-term care setting. J Am Geriatr Soc 1994; 42:28-32.

26. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Choodnovskiy I, Avorn J. Topical glaucoma medications and cardiovascular risk in the elderly. Clin Pharmacol Ther 1994; 55:76-83.

27. Avorn J, Monane M, Gurwitz JH, Glynn RJ, Choodnovskiy I, Lipsitz L. Reduction of bacteriuria and pyuria after ingestion of cranberry juice. JAMA 1994; 271:751-754.

28. Bohn RL, Glynn RJ, Gurwitz JH, Everitt DE, Gilden D, Avorn J. Patterns of glaucoma medication use in the elderly: 1980-1990. J Glaucoma 1994; 3:259-264.

29. Gurwitz JH, Goldberg RJ, Chen Z, Gore J, Alpert JS. Recent trends in hospital mortality of acute myocardial infarction: have improvements been realized for all age groups? The Worcester Heart Attack Study (1975-1990) Arch Intern Med 1994; 154:2202-2208.

30. Rochon PA, Gurwitz JH, Cheung CM, Hayes J, Chalmers TC. Evaluating the quality of articles published in journal supplements compared to those published in the parent journal. JAMA 1994; 272:108-113.

31. Harari D, Gurwitz JH, Choodnovskiy I, Minaker KL, Avorn J. Constipation: assessment and management in an institutionalized elderly population. J Am Geriatr Soc 1994; 42:947-952.

32. Gurwitz JH, Avorn J, Bohn RL, Glynn RJ, Monane M, Mogun H. Initiation of antihypertensive treatment during nonsteroidal anti-inflammatory drug therapy. JAMA 1994; 272:781-786.

33. Gurwitz JH, Field TS, Glynn RJ, Manson JE, Avorn J, Taylor JO, Hennekens CH. Risk factors for non-insulin-dependent diabetes mellitus requiring treatment in the elderly. J Am Geriatr Soc 1994; 42:1235-1240.

34. Avorn J, Bohn R, Mogun H, Gurwitz J, Monane M, Everitt D, Walker A. Neuroleptic drug exposure and treatment of parkinsonism in the elderly: a case-control study. Am J Med 1995; 99:48-54.

35. Monane M, Gurwitz JH, Lipsitz LA, Glynn RJ, Choodnovskiy I, Avorn J. Epidemiologic and diagnostic aspects of bacteriuria: a longitudinal study of elderly women. J Am Geriatr Soc 1995; 43:618-622.

36. Monane M, Glynn RJ, Gurwitz JH, Bohn RL, Levin R, Avorn J. Trends in medication choices for hypertension in the elderly: the decline of the thiazides. Hypertension 1995; 25:1045-1051.

37. Kalish SC, Gurwitz JH, Krumholz HM, Avorn J. A cost-effectiveness model of thrombolytic therapy for acute myocardial infarction. J Gen Intern Med 1995; 10:321-330.

38. Kalish SC, Bohn RL, Mogun H, Gurwitz JH, Avorn J. Antipsychotic prescribing patterns and the treatment of extrapyramidal symptoms in older people. J Am Geriatr Soc 1995; 43:967-973.

39. Avorn J, Gurwitz JH, Bohn RL, Mogun H, Monane M, Walker A. L-dopa therapy following metoclopramide use. JAMA 1995; 274:1780-1782.

40. Harari D, Gurwitz JH, Choodnovskiy I, Avorn J, Minaker KL. Correlates of regular laxative use in frail elderly persons. Am J Med 1995; 99:513-518.

41. Gurwitz JH, McLaughlin TJ, Fish LS. The effect of an Rx-to-OTC switch on medication prescribing patterns and utilization of physician services: the case of vaginal anti-fungal products. Health Services Research 1995; 30:672-685.

42. Weinberg AD, Pols JK, Gurwitz JH. Are antibiotics overutilized for treatment of early stage fevers in long-term care patients? J Subacute Care April 1996;7-10.

43. Col NF, McLauglin TJ, Soumerai SB, Hosmer DW, Yarzebski J, Gurwitz JH, Gore JM, Goldberg RJ. The impact of clinical trials on the use of medications for acute myocardial infarction: results of a community-based study. Arch Intern Med 1996;156:54-60.

44. Gurwitz JH, Everitt DE, Monane M, Glynn RJ, Choodnovskiy I, Beaudet MP, Avorn J. The impact of ibuprofen on the efficacy of antihypertensive treatment with

hydrochlorothiazide in elderly persons. J Gerontol: MEDICAL SCIENCES 1996; 51A:M74-M79.

45. Harari D, Gurwitz JH, Avorn J, Bohn R, Minaker KL. Bowel pattern in relation to age and gender: findings from the National Health Interview Survey and clinical implications. Arch Intern Med 1996; 156:315-320.

46. Gurwitz JH, Gore JM, Goldberg RJ, Rubison M, Chandra N, Rogers WJ, for the participants in the National Registry of Myocardial Infarction. Recent age-related trends in thrombolytic therapy use among patients with acute myocardial infarction. Ann Intern Med 1996; 124:283-291.

47. McLaughlin TJ, Soumerai SB, Willison DJ, Gurwitz JH, Borbas C, Guadagnoli E, McLaughlin B, Morris N, Chun Cheng S, Hauptman PJ, Antman E, Casey L, Asinger R, Gobel F. Adherence to national consensus guidelines for drug treatment of suspected acute myocardial infarction in community hospitals: evidence for undertreatment in women and the elderly. Arch Intern Med 1996; 156:799-805.

48. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. A population-based study of compliance with antihypertensive therapy: role of age, gender, and race. Am J Publ Health 1996;86:1805-1808.

49. Monane M, Gurwitz JH, Bohn RL, Glynn RJ, Levin R, Monette J, Avorn J. The impact of thiazide diuretics on the initiation of lipid-reducing agents in the elderly: a population-based analysis. J Am Geriatr Soc 1997;45:71-75.

50. Chandra H, Yarzebski J, Goldberg RJ, Savageau J, Singleton C, Gurwitz JH, Gore JM. Age-related trends (1986-1993) in the use of thrombolytic agents in patients with acute myocardial infarction: The Worcester Heart Attack Study. Arch Intern Med 1997;157:741-746.

51. McLaughlin TJ, Soumerai SB, Willison DJ, Gurwitz JH, Gao X, Borbas C, Gobel F. The impact of comorbidity on use of thrombolytics and aspirin in acute myocardial infarction. J Gen Intern Med 1997;12:1-6.

52. Harari D, Gurwitz JH, Avorn J, Bohn R, Minaker KL. How do older persons define constipation? Implications for therapeutic management. J Gen Intern Med 1997;12:63-66.

53. Gurwitz JH, Monette J, Rochon PA, Eckler MA, Avorn J. Atrial fibrillation and stroke prevention with warfarin in the long-term care setting. Arch Intern Med 1997;157:978-983.

54. Gurwitz JH, McLaughlin TJ, Willison DJ, Guadagnoli E, Hauptman PJ, Gao X, Soumerai SB. Delayed presentation in patients with acute myocardial infarction. Ann Intern Med 1997;126:593-599.

55. Harari D, Sarkarati M, Gurwitz JH, McGlinchey-Berroth G, Minaker FL. Constipation-related symptoms and bowel program in individuals with spinal cord injury. Spinal Cord 1997;35:394-401.

56. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. The effects of initial drug choice and co-morbidity on antihypertensive therapy compliance: results from a population-based study in the elderly. Am J Hypertension 1997;10:697-704.

57. Monette J, Gurwitz JH, Rochon PA, Avorn J. Physician attitudes concerning warfarin for stroke prevention in atrial fibrillation: results of a survey of long-term care practitioners. J Am Geriatr Soc 1997;45:1060-1065.

58. Guadagnoli E, Shapiro C, Gurwitz JH, Silliman RA, Weeks JC, Borbas C, Soumerai SB. Age-related patterns of care: evidence against ageism in the treatment of early stage breast cancer. J Clin Oncology 1997;15:2338-2344.

59. Gurwitz JH, Kalish SC, Bohn RL, Glynn RJ, Monane M, Mogun H, Avorn J. Thiazide diuretics and the initiation of anti-gout therapy. J Clin Epidemiology 1997;50:953-959.

60. Gurwitz JH, Yeomans SM, Glynn RJ, Lewis BE, Levin R, Avorn J. Patient Noncompliance in the managed care setting: the case of medical therapy for glaucoma. Medical Care 1998;36;357-359.

61. Guadagnoli E, Weeks JC, Shapiro C, Soumerai SB, Gurwitz JH, Borbas C. Use of breast-conserving surgery for treatment of stage I and state II breast cancer. J Clin Oncology 1998;16:101-106.

62. Field TS, Baldor RA, Casey LM, Chuman A, Lasser D, Ehrlich A, Gurwitz JH. Introducing managed care to the medical school curriculum: impact on student attitudes. Am J Managed Care 1998;4:1015-1021.

63. Soumerai SB, McLaughlin TJ, Gurwitz JH, Guadagnoli E, Hauptman PJ, Borbas C, Morris N, McLaughlin B, Gao X, Willison DJ, Asinger R, Gobel F. Effect of local medical opinion leaders on quality of care for acute myocardial infarction, a randomized controlled trial. JAMA 1998;279:1358-1363.

64. Rochon PA, Clark JP, Binns M, Patel V, Gurwitz JH. Reporting of gender specific information in clinical trials of drug therapy for myocardial infarction: CMAJ 1998;159:321-327.

65. Goldberg RJ, Mooradd M, Gurwitz JH, Rogers WJ, French WJ, Barron HV, Gore JM. Impact of time to treatment with tissue plasminogen activator on morbidity and mortality following acute myocardial infarction (The Second National Registry of Myocardial Infarction) Am J Cardiol 1998;82:259-264.

66. Guadagnoli E, Shapiro CL, Weeks JC, Gurwitz JH, Borbas C, Soumerai SB. The quality of care for treatment of early-stage breast cancer: Is it consistent with national guidelines? Cancer 1998;83:302-309.

67. Willison DJ, Soumerai SB, McLaughlin TJ, Gurwitz JH, Gao X, Guadagnoli E, Pearson S, Hauptman P, McLaughlin B. Consultation between cardiologists and generalists in the management of acute myocardial infarction: implications for quality of care. Arch Intern Med 1998;158:1778-1783.

68. Goldberg RJ, McCormick D, Gurwitz JH, Yarzebski J, Lessard D, Gore JM. Age-related trends in short and long-term survival following acute myocardial infarction: a twenty-year population-based perspective (1975-1995). Am J Cardiol 1998;82:1311-1317.

69. Gurwitz JH, Gore JM, Goldberg RJ, Barron HV, Breen T, Rundle AC, Sloan MA, French W, Rogers WJ. Risk for intracranial hemorrhage after tissue plasminogen activator treatment for acute myocardial infarction. Participants in the National Registry of Myocardial Infarction 2. Ann Intern Med 1998;129:597-604.

70. Donahue JG, Andrade SE, Cain EM, Defore TA, Goodman MJ, Gurwitz JH, Platt R. Lamotrigine and severe skin eruptions. Pharmacoepidemiology and Drug Safety 1998;7:415-417.

71. Rochon PA, Clark JP, Binns MA, Patel V, Gurwitz JH. Reporting of gender-related information in clinical trials of drug therapy for myocardial infarction. CMAJ 1998;159:321-7.

72. Goldberg RJ, Mooradd M, Gurwitz JH, Rogers WJ, French WJ, Barron HV, Gore JM. Impact of time to treatment with tissue plasminogen activator on morbidity and mortality following acute myocardial infarction (The second National Registry of Myocardial Infarction). Am J Cardiol 1998;82:259-64.

73. Lasser D, Chuman A, Ferrara E, Gurwitz JH. Use of a mini-grant program to stimulate generalist training in a university community. Acad Med 1999;74 (1 suppl):S30-S35.

74. Andrade SE, Gurwitz JH, Fish LS. The effect of an Rx-to-OTC switch on medication prescribing patterns and utilization of physician services: the case of H2-receptor antagonists. Med Care 1999;37:424-430.

75. Glynn RJ, Monane M, Gurwitz JH, Choodnovskiy I, Avorn J. Agreement between drug treatment and a discharge diagnosis of diabetes mellitus in the elderly. Am J Epidemiology 1999;149:541-9.

76. McCormick D, Gurwitz JH, Lessard D, Yarzebski J, Gore JM, Goldberg RJ. Use of aspirin, beta blockers, and lipid lowering medications before recurrent acute myocardial infarction: Missed opportunities in prevention? Arch Intern Med 1999;159:561-567.

77. Field TS, Gurwitz JH, Glynn RJ, Salive ME, Gaziano JM, Taylor JO, Hennekens CH. The renal effects of nonsteroidal anti-inflammatory drugs in the elderly: findings from the established populations for epidemiologic studies of the elderly. J Am Geriatr Soc 1999;47:507-511.

78. McCormick D, Gurwitz JH, Savageau J, Yarzebski J, Gore JM, Goldberg RJ. Differences in discharge medication after acute myocardial infarction in patients with HMO and fee-for-service medical insurance. J Gen Intern Med 1999;14:73-81.

79. Andrade SE, Gurwitz JH, Fish LS. The effect of an Rx-to-OTC switch on medication prescribing patterns and utilization of physician services: the case of H2-receptor antagonists. Med Care 1999;37:424-430.

80. Goldberg RJ, Samad NA, Yarzebski J, Gurwitz J, Bigelow C, Gore JM. Temporal trends in cardiogenic shock complicating acute myocardial infarction. N Engl J Med 1999;340:1162-8.

81. Glynn RJ, Monane M, Gurwitz JH, Choodnovskiy I, Avorn J. Agreement between drug treatment data and a discharge diagnosis of diabetes mellitus in the elderly. Am J Epidemiol 1999;149:541-9.

82. Soumerai SB, McLaughlin TJ, Gurwitz JH, Pearson S, Christiansen C, Borbas C, Morris N, McLaughlin B, Gao Xiaoming, Ross-Degnan D. Timeliness and quality of care for elderly patients with acute myocardial infarction under HMO vs. fee-for service insurance. Arch Intern Med 1999;159:2013-2020.

83. Goldberg RJ, Gurwitz JH, Gore JM. Duration of, and temporal trends (1994-1997) in, prehospital delay in patients with acute myocardial infarction: The Second National Registry of Myocardial Infarction. Arch Intern Med 1999;159:2141-2147.

84. Glynn RJ, Monane M, Gurwitz JH, Choodnovskiy I, Avorn J. Aging, comorbidity and reduced rates of drug treatment for diabetes mellitus. J Clin Epidemiol 1999;52:781-790.

85. Majumdar SR, Gurwitz JH, Soumerai SB. Undertreatment of hyperlipidemia in the secondary prevention of coronary artery disease. J Gen Intern Med 1999;12:711-717.

86. Rochon PA, Anderson GM, Tu JV, Gurwitz JH, Clark JP, Shear NH, Lau P. Age- and gender-related use of low-dose therapy: the need to manufacture low-dose therapy and evaluate the minimum effective dose. J Am Geriatr Soc 1999;47:954-959.

87. McLaughlin TJ, Gurwitz JH, Willison DJ, Gao X, Soumerai SB. Delayed thrombolytic treatment of elderly patients with acute myocardial infarction. J Am Geriatr Soc 1999;47:1222-1228.

88. Rochon PA, Anderson GM, Tu JV, Clark JP, Gurwitz JH, Szalai JP, Lau P. Use of beta-blocker therapy after acute myocardial infarction in Ontario. CMAJ 1999;161:1403-1408.

89. Brass LM, Lichtman JH, Wang Y, Gurwitz JH, Radford MJ, Krumholz HM. Intracranial hemorrhage associated with thrombolytic therapy for elderly patients with acute myocardial infarction. Results from the Cooperative Cardiovascular Project. Stroke 2000;31:1802-1811.

90. Barron HV, Rundle A, Gore JM, Gurwitz JH, Penney T. Intracranial hemorrhage rates and effect of immediate beta-blocker use in patients with acute myocardial infarction treated with tissue plasminogen activator. Am J Cardiology 2000;85:294-298.

91. Bohn RL, Gurwitz JH, Yeomans SM, Glynn RJ, Pasquale LR, Walker AM, Avorn J. Which patients are treated for glaucoma? An observational analysis. J Glaucoma 2000;9:38-44.

92. Chan KA, Andrade SE, Boles M, Buist DSM, Chase GA, Donahue JG, Goodman MJ, Gurwitz JH, LaCroix AZ, Platt R. HMG-CoA reductase inhibitors and reduced risk of fracture among older women. The Lancet 2000;355:2185-2188.

93. Andrade SE, Gurwitz JH, Cernieux J, Fish LS. Evaluation of a formulary switch from conjugated to a esterified estrogens in a managed care setting. Medical Care 2000;38:970-975.

94. Gurwitz JH, Field T, Avorn J, McCormick D, Jain S, Eckler M, Benser B, Edmonson AC, Bates DW. Incidence and preventability of adverse drug events in the nursing home setting. Am J Med 2000;109:87-94.

95. Guadagnoli E, Soumerai SB, Gurwitz JH, Borbas C, Shapiro CL, Weeks JC, Morris N. Improving discussion of surgical treatment options for patients with breast

cancer: local medical opinion leaders versus performance feedback. Breast Cancer Research and Treatment 2000;61:171-175.

96. Rochon PA, Tu JV, Anderson GM, Gurwitz JH, Clark JP, Lau P, Czalai JP, Sykora K, Naylor D. Rate of heart failure and equivalent 1-year survival for older people receiving low-dose beta-blocker therapy after myocardial infarction. The Lancet 2000;356:639-644.

97. Harrold LR, Yood RA, Andrade SE, Reed JI, Cernieux J, Straus W, Weeks M, Lewis B, Gurwitz JH, Evaluating the predictive value of osteoarthritis diagnoses in an administrative database. Arthritis Rheum 2000;43:1881-1885.

98. Harrold LR, Gurwitz JH, Field TS, Andrade SE, Fish LS, Jarry PD, Yood R. The diffusion of a novel therapy into clinical practice: the case of sildenafil. Arch Intern Med 2000;160:3401-3405.

99. Smalley W, Shatin D, Wysowski DK, Gurwitz J, Andrade SE, Goodman M, Chan KA, Platt R, Schech SD, Ray WA. Contraindicated use of cisapride: the impact of an FDA regulatory action. JAMA 2000; 284:3036-3039.

100. Goldberg RJ, Gore JM, Thompson CA, Gurwitz JH. Recent magnitude of, and temporal trends (1994-1997) in the incidence and hospital death rates of cardiogenic shock complicating acute myocardial infarction: the Second National Registry of Myocardial Infarction. Am Heart J 2001;141:65-71.

101. Majumdar SR, Inui TS, Gurwitz JH, Gillman MW, McLaughlin TJ, Soumerai SB. Influence of physician specialty on adoption and relinquishment of calcium channel blockers, and other treatments for myocardial infarction. J Gen Intern Med 2001;16:351-359.

102. Yood R, Harrold L, Fish L, Cernieux J, Emani S, Conboy B, Gurwitz J. Prevention of glucocorticoid-induced osteoporosis: Experience in a managed care setting. Arch Intern Med 2001;161:1322-1327.

103. Angeja BG, Rundle AC, Gurwitz JH, Gore JM, Barron JV. Death or non-fatal stroke in patients with acute myocardial infarction treated with tissue plasminogen activator. Am J Cardio 2001;87:627-630.

104. Field TS, Gurwitz JH, Avorn J, McCormick D, Jain S, Eckler M, Benser M, Bates DW. Risk factors for adverse drug events among nursing home residents. Arch Intern Med 2001;161:1629-1634.

105. McCormick D, Gurwitz JH, Goldberg RJ, Becker R, Tate JP, Elwell A, Radford MJ. Prevalence and quality of warfarin use for patients with atrial fibrillation in the long-term care setting. Arch Intern Med 2001;161:2458-2463.

106. Baldor RA, Field TS, Gurwitz JH. Using the "Question of Scruples" game to teach managed care ethics to medical students. Acad Med 2001;76:510-511.

107. Gurwitz JH, Guadagnoli E, Landrum MB, Silliman RA, Wolf R, Weeks JC. The treating physician as active gatekeeper in the recruitment of research subjects. Med Care 2001;39:1339-1344.

108. Putnam KG, Buist DSM, Fishman P, Andrade SE, Boles M, Chase GA, Goodman MJ, Gurwitz JH, Platt R, Raebel MA, Chan KA. Chronic disease score as a predictor of subsequent hospitalization. Epidemiology 2002;12:340-346.

109. Silliman RA, Guadagnoli, E, Rakowski W, Landrum MB, Lash TL, Wolf R, Fink A, Ganz PA, Gurwitz J, Borbas C, Mor V. Adjuvant tamoxifen prescription in women 65 years and older with primary breast cancer. J Clin Oncol 2002;20:2680-2688.

110. Andrade SE, Gurwitz JH, Drug benefit plans under managed care: to what extent do older subscribers selecting less drug coverage put themselves at increased financial risk? J Am Geriatr Soc 2002;50:178-181.

111. Gurwitz JH, Goldberg RJ, Malmgren JA, Barron HV, Tiefenbrunn AJ, Frederick PD, Gore JM. Hospital transfer of patients with acute myocardial infarction: the effects of age, race and insurance type. Am J Med 2002;112:528-534.

112. Andrade SE, Gurwitz JH, Chan KA, Donahue JG, Beck A, Boles M, Buist DSM, Goodman M, LaCroix AZ, Levin TR, Platt R. Validation of diagnoses of peptic ulcers and bleeding from administrative databases: a multi-health maintenance organization study. J Clin Epi 2002;55:310-313.

113. Harrold LR, Yood RA, Straus W, Andrade SE, Reed JI, Cernieux J, Lewis B, Gurwitz JH. The challenges of estimating health service utilization for osteoarthritis patients on a population-level. J Rheum 2002;29:1931-1936.

114. Donahue JG, Chan KA, Andrade SE, Beck A, Boles M, Buist DSM, Carey VJ, Chandler JM, Chase GA, Ettinger B, Fishman P, Goodman M, Guess HA, Gurwitz JH, LaCroix AZ, Levin TR, Platt R: Gastric and duodenal safety of alendronate. Arch Intern Med 2002;162:936-942.

115. Soumerai SB, McLaughlin TJ, Ross-Degnan D, Christiansen CL, Gurwitz JH. Effectiveness of thrombolytic therapy for acute myocardial infarction in the elderly. Arch Intern Med 2002;162;561-568.

116. Mazor KM, Campbell EG, Field T, Purwono V, Peterson D, Lockwood JH, Weissman JS, Gurwitz JH. Managed care education: what medical students are telling us. Acad Med 2002;77:1128-1133.

117. Rochon PA, Bero LA, Bay AM, Gold JL, Dergal JM, Binns MA, Streiner DL, Gurwitz JH. Comparing review articles published in peer-reviewed and throwaway journals. JAMA 2002;287:2853-2856.

118. Keough M, Field TS, Gurwitz JH. A model of community-based interdisciplinary team training in the care of the frail elderly. Acad Med 2002;77:936.

119. Mazor KM, Clauser BE, Field T, Yood R, Gurwitz JH. A demonstration of the impact of response bias on the results of patient satisfaction surveys. Health Services Research 2002;37:1403-1417.

120. Chan KA, Truman A, Gurwitz JH, Hurley JS, Martinson B, Platt R, Everhart J, Moseley R, Terrault N, Ackerson L, Selby JV. A cohort study of the incidence of acute liver failure in diabetic patients treated with hypoglycemic agents. Arch Intern Med (in press).

Reviews and/or Book Chapters:

1. Gurwitz JH, Soumerai SB, Avorn J. Improving medication prescribing and utilization in the nursing home. J Am Geriatr Soc 1990; 38:542-552.

2. Gurwitz JH, Avorn J. Adverse drug reactions: Old Age -- Is it a risk factor? Agents and Actions Supplements 1990; 29:13-25.

3. Avorn J, Gurwitz JH. Principles of Geriatric Pharmacology. In: Geriatric Medicine, Second Edition. Cassel CK, Riesenberg DE, Sorensen LB, Walsh JR, eds.; Springer-Verlag, New York, 1990, pages 65-77.

4. Gurwitz JH, Goldberg RJ, Gore JM. Coronary thrombolysis for the elderly? JAMA 1991; 265:1720-1723.

5. Gurwitz JH, Avorn J. The ambiguous relation between aging and adverse drug reactions. Ann Intern Med 1991; 114:956-966.

6. Ray WA, Gurwitz J, Decker MD, Kennedy DL. Effects of prescribed medications on the safety of older drivers. Human Factors 1992; 34:33-47.

7. Gurwitz JH. The FDA guideline for the study of drugs in the elderly. The perspective of the investigator and clinician. In: Inclusion of Elderly in Clinical Trials: Cardiovascular Disease and Cardiovascular Therapy as a

Model. Wenger, NK, ed.; Marion Merrell Dow Inc., Kansas City, 1993:205-212.

8. Monane M, Gurwitz JH, Monane S, Avorn J. Compliance issues in medical practice. Hospital Physician 1993; 29:35-39.

9. Kalish S, Gurwitz JH, Avorn J. Anticoagulant therapy in the elderly. Primary Cardiology 1993; 7:34-42.

10. Monane M, Gurwitz JH, Avorn J. Pharmacotherapy in with psychoactive medications in long-term care: challenges, management and future directions. Generations 1993; 17:57-60.

11. Harari D, Gurwitz JH, Minaker KL. Constipation in the elderly. J Am Geriatr Soc 1993; 41:1130-1140.

12. Jansen RWMM, Gurwitz JH. Controversies surrounding the use of beta-blocker therapy in elderly patients with cardiovascular disease. Drugs and Aging 1994; 4:175-183.

13. Gurwitz JH, Avorn J. Improving pharmacotherapeutic decision-making in the care of older patients. In: Developing expertise in geriatric drug therapy. Abrams, WB (ed.); Merck Company Foundation., Whitehouse Station, 1993:19-26.

14. Monane M, Gurwitz JH, Avorn J. Pharmacotherapy in with psychoactive medications in long-term care: challenges, management and future directions. In: Mental health and aging. Smyer, MA, ed.; Springer Publishing Co., Inc., New York, 1993.

15. Gurwitz JH. Suboptimal medication use in the elderly: Just the tip of the iceberg. JAMA 1994; 272:316-317.

16. Rochon PA, Gurwitz JH. Geriatrics septet: drug therapy. Lancet 1995; 346:32-36.

17. Gurwitz JH. Unconventional medicine and Alzheimer's disease. J Am Geriatr Soc 1995; 43: 829-830.

18. Avorn J, Gurwitz JH. Drug use in the nursing home. Ann Intern Med 1995; 123:195-204.

19. Monette J, Gurwitz JH, Avorn J. Epidemiology of adverse drug events in the nursing home setting. Drugs and Aging 1995; 7:203-211.

20. Avorn J, Gurwitz JH, Drug use. In: Medical Care of the Nursing Home Resident: What Physicians Need to Know. Besdine RW, Rubenstein LZ, Snyder L, eds., American College of Physicians, Philadelphia, 1996: 77-90.

21. Gurwitz JH. Using pharmacoepidemiological findings to guide clinical practice: sulfonylureas and hypoglycemia in older adults. J Am Geriatr Soc 1996; 44:871-872.

22. Avorn J, Gurwitz JH. Principles of Geriatric Pharmacology. In: Geriatric Medicine, Third Edition. Cassel, Cohen, Larson, Meier, Resnick, Rubenstein, Sorensen, eds.; Springer-Verlag, New York 1997;66-77.

23. Gurwitz JH, Monane M, Monane S, Avorn J. Polypharmacy. In: Quality Care for the Nursing Home Resident. Lipsitz LA, Morris JN, Murphy K, Belleville-Taylor P. eds.; Mosby Lifeline, St. Louis, 1997: 13-25.

24. Gurwitz JH, Rochon P, Avorn J. Optimal drug therapy in the elderly. Federal Practitioner 1996;13: 15-32.

25. Rochon PA, Gurwitz JH. Geriatric update 1996: The age of women. Lancet 1996; 348 (suppl II): 8.

26. Solomon DH, Gurwitz JH. Toxicity of nonsteroidal anti-inflammatory drugs in the elderly: Is advanced age a risk factor? Am J Med 1997;102:208-215.

27. Gurwitz JH, Goldberg RJ. Coronary thrombolysis for the elderly: Is clinical practice really lagging behind evidence of benefit? JAMA 1997;277:1723-1724.

28. Andrade S, Gurwitz JH. Pharmacoepidemiology and the elderly. In: Crome P. Ford G, eds.; Imperial College Press (in press)

29. Gurwitz JH, Rochon P, Avorn J. Optimizing drug therapy in the elderly. P & T 1997;22:331-347. (reprinted from Federal Practitioner 1996;13:15-32)

30. Rochon PA, Gurwitz JH. Optimizing drug treatment for elderly people: The prescribing cascade. BMJ 1997;315:1096-1099.

31. McCormick D, Goldberg R, Gurwitz JH. Anticoagulation in the elderly. J Thrombosis and Thombolysis 1999;7:157-163.

32. Goldberg RJ, Gurwitz JH. Disseminating the results of clinical trials to community-based practitioners: Is anyone listening? Am Heart J 1999;137:4-7.

33. Vestal RE, Gurwitz JH. Drugs in special populations: the elderly. In: Melmon and Morrelli's Clinical Pharmacology: Basic Principles in Therapeutics, Fourth Edition. Melmon KL, Morrelli HF, Hoffman BB, Nierenberg DW, eds: McGraw-Hill, Inc., New York. 2000

34. Rochon PA, Clark JP, Gurwitz JH. Challenges of prescribing low-dose drug therapy for older people. CMAJ 1999;160:1029-31.

35. Rochon PA, Gurwitz JH. Prescribing for seniors: neither too much nor too little. JAMA 1999;282:113-115.

36. Barron HV, Rundle A, Gurwitz J, Tiefenbrunn A. Reperfusion therapy for acute myocardial infarction: Observations from the National Registry of Myocardial Infarction 2 (NRMI 2). Cardiology in Review 1999;7:156-160.

37. Harrold LH, Field TS, Gurwitz JH. Knowledge, patterns of care and outcomes of care for generalists and specialists. J Gen Intern Med 1999;14:499-511.

38. Gurwitz JH, Rochon PA. Health care quality, the elderly patient, and the primary care physician. J Am Geriatr Soc 1999;47:1473-1474.

39. Gurwitz JH, Rochon PA. Medication use in the elderly. In: Levkoff SE, Chee YK, (eds) Aging in good health: Multidisciplinary Perspectives, Springer, New York 2000.

40. Gurwitz JH. Considerations in designing an ideal medication-use system: lessons from caring for the elderly. Am J Health-Syst Pharm 2000;57:548-551.

41. Andrade S, Gurwitz J, Pharmacoepidemiology and the elderly. In: Crome P, Ford G. Drugs and the older population. Imperial College Press, London 2000.

42. Platt R, Barrett PH, Durham ML, Gurwitz J, Kilkenny R, Wagner E,. HMO-academic health center partnerships. In: For the Health of the Public: Ensuring the Future of Clinical Research. Meyer RE, ed. Association of American Medical Colleges, Washington, DC, 2000.

43. Platt R, Davis R, Finkelstein J, Go AS, Gurwitz JH, Roblin D, Soumerai S, Ross-Degnan D, Andrade S, Goodman MJ, Martinson B, Raebel MA, Smith D. Ulcickas-Yood M, Chan A. Multcenter Epidemiologic and Health Services Research on Therapeutics in the HMO Research Network Center for Education and Research on Therapeutics (CERT). Pharmacoepidemiol Drug Saf 2001;10:373-377.

44. Rochon PA, Bronskill SE, Gurwitz JH. Health care for older people. British Medical Journal 2002;324:1231-1232.

45. Rochon PA, Gurwitz JH. Medication use. In: Hazzard WR, Blass JP, Halter JB, Ouslander JG, Tinetti ME, eds. Principles of Geriatric Medicine and Gerontology, 5th edition. McGraw-Hill, New York, NY (in press).

46. Gurwitz JH, Rochon PA. Improving the quality of medication use in the elderly: a not so simple prescription. Arch Intern Med (in press).

47. Avorn J, Gurwitz JH, Rochon PA. Principles of Geriatric Pharmacology. In: Geriatric Medicine, Fourth Edition. Cassel, Cohen, Larson, Meier, Resnick, Rubenstein, Sorensen, eds; Springer-Verlong, New York (in press).

Educationally Relevant Publications:

1. Gurwitz J, Kelly R. A broken heart. Pharmacology Block Case Study New Pathway Curriculum, Harvard Medical School, 1992.

2. Gurwitz JH, Monane M, Avorn J. Principles of Pharmacology. In: Geriatrics Review Syllabus Supplement Reuben DB, Yoshikawa TT, Besdine RW, eds. American Geriatrics Society; New York, 1993.

3. Gurwitz JH, Monane M, Avorn J. Polypharmacy. In: Geriatrics Review Syllabus (1993-1994) Reuben DB, Yoshikawa TT, Besdine RW, eds. American Geriatrics Society; New York, 1993.

4. Gurwitz JH, Wolfe MM. H_2 blockers: too much of a good thing? Brigham and Women's Hospital Medication Education and Management Program.

Non-Print Materials:

1. Gurwitz JH. Drug use in the elderly. (CD-ROM) In: Michael K. Rees, Core Curriculum in Primary Care- Preventive Medicine Section. Silver Platter Education, Inc. Multimedia Accelerated Learning. Norwood, MA 1995.

Commentaries, Letters, Book Reviews:

1. Gurwitz JH. Book review: Timiras PS. Physiological Basis of Geriatrics. New York, Macmillan, 1988. N Engl J Med 1989; 320:471.

2. Gurwitz JH. Commentary to: Greenblatt DJ, Harmatz JS, Shapiro L, et al. Sensitivity to triazolam in the elderly. NEJM 1991; 324:1691-8. ACP Journal Club (A supplement to Annals of Internal Medicine) 1991; 115(Suppl 6):94.

3. Gurwitz JH. Commentary to: Lipton HL, Bero LA, Bird JA, McPhee SJ. The impact of clinical pharmacists' consultations on physicians' geriatric drug prescribing. A randomized controlled trial. Med Care 1992; 30:646-58. ACP Journal Club (A supplement to Annals of Internal Medicine) 1993; 118(Suppl 1):29.

4. Gurwitz JH, Avorn J, Ansell J. Aging and warfarin therapy. Ann Intern Med 1992; 117:879.

5. Monane M, Gurwitz JH, Avorn J. New books on medication use and the elderly. The Gerontologist 1994; 34:272-274.

6. Avorn J, Monane M, Gurwitz JH, Glynn RI, Choodnovskiiy I, Lipsitz LA. Reduction of bacteriuria and pyuria using cranberry juice. JAMA 1994; 272:589.

7. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Avorn J. Heart failure and noncompliance in the elderly. Arch Intern Med 1994; 154:2109-2110.

8. Ross-Degnan D, Soumerai SB, Fortess EE, Gurwitz JH. Withdrawal of a drug from the market: what should the prescriber do? JAMA 1994; 272:1253.

9. Rochon PA, Gurwitz JH, Chalmers TC. Too many words? Mozart 1, Emperor 0. JAMA 1995; 273:1088.

10. Gurwitz JH. Start low and go slow: dosing of antipsychotic medications in elderly patients with dementia. Arch Intern Med 1995; 155:2017-2018.

11. Avorn J, Gurwitz JH. Drug use in the nursing home. Ann Intern Med 1996; 124:616.

12. Gurwitz JH. Expert commentary on the ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction. Abstracts of Clinical Care Guidelines (A Joint Commission Newsletter) 1997;9:7-8.

13. Gurwitz JH. Warfarin therapy in the nursing home. Arch Intern Med 1997;157:2665.

14. Gurwitz JH. Thrombolytic therapy for elderly patients. JAMA 1997;278:1402.

15. Gurwitz JH. Warfarin treatment. J Am Geriatr Soc 1998;46:927-928.

16. Gurwitz JH. Commentary to: Borbone F, McMahon AD, Davey PG, et al. Associations between road-traffic accidents with benzodiazepine use. Lancet 1998;352:1331-6. ACP Journal Club (March/April 1999);48.

17. Gurwitz JH, Goldberg RJ, Gore JM. Coronary thrombolysis: a double-edged sword? Ann Intern Med 1999;131:71.

18. Rochon PA, Gurwitz JH. Prescribing for elderly persons. JAMA 2000;283:339-340.

Abstracts:

A1. Avorn J, Everitt DE, Bright RA, Gurwitz J, Chown M. AIDS-related diagnoses and drug use among AZT users in New Jersey Medicaid. J Clin Res Drug Dev 1989; 3:203.

A2. Field TS, Glynn RJ, Gurwitz JH, Manson JE, Taylor JO, Hennekens CH. Independence of Hemoglobin A_1C and cardiovascular risk factors in an elderly population. Gerontologist 1993; 33(Special Issue II):11.

A3. Harari D, Gurwitz J. Self-reported fecal incontinence and perianal fecal staining in institutionalized elderly. Gerontologist 1993; 33(Special Issue II):51.

A4. Weinberg AD, Pals JK, Gurwitz JH, Minaker KL. Patterns of antibiotic utilization in early febrile illness in long-term care patients. 1994 Annual Meeting of the Gerontological Society of America. The Gerontologist 1994; 34(Special Issue II):16.

A5. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Mogun H, Avorn J. Predictors of hospital admission for congestive heart failure in the elderly: the paradox of medication compliance. J Am Geriatr Soc 1994; 42:SA45.

A6. Harari D, Sarkarati M, Gurwitz JH, Grande L, Brown S, McGlinchy-Berroth R, Minaker KL. Use of abdominal radiographs to assess fecal retention in patients with spinal cord injury. J Am Paraplegia Soc 1994; 17:207.

A7. Gurwitz JH, Bohn RL, Kalish SC, Monane M, Glynn RJ, Mogun H, Avorn J. Thiazide diuretics and the initiation of anti-gout therapy in the elderly. Clin Pharmacol Ther 1995; 57:198.

A8. Monette J, Gurwitz JH, Rochon PA, Eckler MA, Avorn J. Use of warfarin in the frail elderly with atrial fibrillation. Clin Pharmacol Ther 1995; 57:198.

A9. Monane M, Gurwitz JH, Bohn RL, Glynn RJ, Levin R, Monette J, Avorn J. The impact of thiazides on the initiation of lipid-reducing agents in the elderly. Clin Pharmacol Ther 1995; 57:198.

A10. Harari D, Gurwitz JH, Bohn RL, Avorn J. How do elderly persons define constipation? 1995 Annual Meeting of the Gerontological Society of America.

A11. Field TS, Gurwitz JH, Glynn RJ, Salive ME, Chrischilles EA, Taylor JO, Hennekens CH. The renal effects of non-steroidal anti-inflammatory agents in the elderly. 1995 Annual Meeting of the Gerontological Society of America.

A12. Monane M, Bohn RL, Glynn RJ, Gurwitz JH, Avorn J. A population-based study of compliance with antihypertensive therapy: role of age, race, and gender. 1995 Annual Meeting of the International Society for Pharmacoepidemiology.

A13. Yeomans SM, Gurwitz JH, Glynn RJ, Avorn J. Initiation of drug therapy to treat glaucoma in a large managed care patient population. 1995 Annual Meeting of the American Academy of Ophthalmology.

A14. Gurwitz JH, Yeomans SM, Lewis B, Glynn RJ, Avorn J. Treatment for glaucoma: adherence by older persons in managed care. 1996 Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics Clin Pharmacol Ther 1996; 59:172.

A15. Monette J, Gurwitz JH, Rochon P, Glynn RJ, Avorn J. Warfarin in the frail elderly with atrial fibrillation: results of a physician survey. 1996 Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics. Clin Pharmacol Ther 1996; 59:173.

A16. Gurwitz JH, Monette J, Rochon P, Eckler MA, Avorn J. Atrial fibrillation in the long-term care setting. J Am Geriatr Soc 1996:44:S20.

A17. Monette J, Gurwitz JH, Rochon P, Avorn J. Physicians' knowledge and attitudes regarding the use of warfarin in frail elderly patients with atrial fibrillation. J Am Geriatr Soc 1996;44:S22.

A18. Gurwitz JH, McLaughlin TJ, Willison DJ, Guadagnoli E, Hauptman PJ, Gao X, Soumerai SB. Patient age and late hospital arrival in acute myocardial infarction. J Am Geriatr Soc 1996;44:S20.

A19. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. A population-based study of compliance with antihypertensive therapy: role of drug choices and comorbidity. J Am Geriatr Soc 1996;44:S44.

A20. Gurwitz JH, Gore J, Goldberg RJ, Rubison M, Magnuson D, French W, Rogers W. Age-related risks of hemorrhagic stroke with rTPA treatment in acute myocardial infarction: findings from the National Registry of Myocardial Infarction. Pharmacoepidemiology and Drug Safety 1996; 5 (suppl 1): S52

A21. Willison D, Soumerai SB, McLaughlin T, Gurwitz J, Gao X, Guadagnoli E, Pearson S, Hauptman P, McLaughlin B. Cardiologist and generalist involvement in the care of acute MI- implications for quality. 1996 Annual Meeting of the Association for Health Services Research.

A22. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Mogun H, Avorn J. The impact of thiazides on the initiation of anti-arrhythmic agents in the elderly. Clin Pharm Ther 1997;61:174.

A23. Gurwitz JH, Gore J, Goldberg R, Barron H, Breen T, Hilbe J, French W, Rogers W. Risk factors for intracranial hemorrhage with TPA treatment in acute myocardial infarction. JGIM 1997;12 April (supplement): 53.

A24. McLaughlin TJ, Gurwitz JH, Gao X, Soumerai SB. Delayed thrombolysis in patients with acute myocardial infarction. JGIM 1997;12 April (supplement): 76.

A25. McLaughlin, Gurwitz JH, Guadagnoli E, Hauptman P. A randomized trial of opinion leader education plus performance feedback to improve quality of care for acute MI. JGIM 1997;12 April (supplement):80.

A26. McCormick D, Gurwitz JH, Savageau J, Yarzebski J, Gore JM, Goldberg RJ. Differences in discharge medication regimens for acute myocardial infarction in patients with HMO vs fee-for-service insurance plans. JGIM 1997;12 April (supplement):84.

A27. Baldor RA, Field TS, Casey L, Lasser D. Ehrlich A, Chuman AB, Gurwitz JH. An interclerskip on managed care for third year medical students. Thirty-sixth Annual Conference on Research in Medical Education (RIME).

A28. Bohn R, Gurwitz J, Yeomans S, Glynn R, Pasquale L, Avorn J. Clinical characteristics of a cohort of patients newly initiated on chronic glaucoma therapy. 13th International Conference on Pharmacoepidemiology.

A29. Goldberg RJ, Gurwitz JH, McCormick D, Yarzebski JL, Savageau J, Gore JM. Impact of advanced age on, and temporal trends in, prognosis following acute myocardial infarction: a community-wide perspective. 70th Scientific Session of American Heart Association.

A30. Lindblad P, Field T, Straus J, Smiley E, Wright M, Gurwitz JH. Primary care and specialists: an evolving relationship - The Fallon University Project. Fourth Annual Meeting of the Generalist Physician Initiative.

A31. Sloan MA, Pirzada SR, Ornato J, Gurwitz JH, Gore JM, Tiefenbrunn AJ, French WJ, Weaver WD, Rogers WJ. The rate of ischemic stroke following acute

myocardial infarction is decreasing. The National Registry of Myocardial Infarction Experience. 47th Annual Scientific Session of the American College of Cardiology.

A32. Andrade SE, Gurwitz JH, Fish, LS. The effect of an Rx-to-OTC switch on medication prescribing patterns and utilization of physician services: the case of H_2-receptor antagonists. 1998 American Association of Health Plans/HMO Research Network Conference.

A33. Field T, Mazor K, Lessard D, Lindblad P, Gurwitz JH. Patient-satisfaction with primary care physicians and rates of referrals to specialists. 1998 American Association of Health Plans/HMO Research Network Conference.

A34. Gurwitz JH, Field T, Avorn J, McCormick D, Jain S, Eckler M, Benser M, Bates DW. Incidence and preventability of adverse drug events in the nursing home setting. Society of General Internal Medicine, 21st Annual Meeting, April 1998.

A35. McCormick D, Gurwitz JH, Lessard D, Yarzebski J, Gore JM, Goldberg RJ. Use of aspirin, beta blockers and lipid lowering medications prior to recurrent myocardial infarction: missed opportunities for secondary prevention. Society of General Internal Medicine, 21st Annual Meeting, April 1998.

A36. Majumdar SR, Gurwitz JH, Soumerai SB. Undertreatment of hyperlipidemia in the secondary prevention of coronary artery disease. Society of General Internal Medicine, 21st Annual Meeting, April 1998.

A37. Soumerai SB, McLaughlin TJ, Gurwitz JH, Pearson S, Christiansen C, Gao X, Ross-Degnan D. Quality of care for acute MI among elderly patients in medicare HMOs vs. fee-for-service insurance. Society of General Internal Medicine, 21st Annual Meeting, April 1998.

A38. Markson LJ, Weinstein B, Alper E, Gurwitz JH. Effect of a nurse-practitioner-covered medical inpatient service on housetaff clinical experience. Society of General Internal Medicine, 21st Annual Meeting, April 1998.

A39. Gurwitz JH, Andrade SE, Fish LS, Cernieux J, Yood R. Evaluation of a comprehensive formulary switch in the managed care setting: The case of hormone replacement therapy. 1999 American Association of Health Plans/HMO Research Network Conference.

A40. Harrold L, Gurwitz JH, Field T, Andrade SE, Fish LS, Jarry PD, Yood D. The Diffusion of a novel therapy into general medical practice: the case of sildenafil. 1999 American Association of Health Plans/HMO Research Network Conference.

A41. Field T, Gurwitz JH, Avorn J, McCormick D, Jain S, Eckler M, Benser M, Edmondson AC, Bates DW. Incidence and preventability of adverse drug events in

the nursing home setting. 1999 American Association of Health Plans/HMO Research Network Conference.

A42. Yood R, Harrold L, Reed J, Andrade S, Cernieux J, Lewis B, Straus W, Weeks M. Gurwitz JH. Validation of osteoarthritis diagnoses in an administrative database. 1999 American Association of Health Plans/HMO Research Network Conference.

A43. Gurwitz JH, Guadagnoli E, Silliman R, Weeks JC. The treating physician as active gatekeeper in the recruitment of research subjects. Society of General Internal Medicine, 22nd Annual Meeting, April 1999.

A44. Gurwitz JH, Goldberg RJ, Elwell A, Radford MJ. Prevalence and quality of warfarin use for patients with atrial fibrillation in the long-term care setting. Society of General Internal Medicine, 22nd Annual Meeting, April 1999.

A45. Harrold L, Yood R, Reed J, Andrade S, Cernieux J, Lewis B, Straus W, Weeks M, Gurwitz JH. Validation of osteoarthritis diagnoses in an administrative database. Society of General Internal Medicine, 22nd Annual Meeting, April 1999.

A46. Mazor KM, Field TS, Gurwitz JH, Hatem D. Do HMO staff physicians who precept differ from physicians who do not? Society of General Internal Medicine, 22nd Annual Meeting, April 1999.

A47. Mazor KM, Field TS, Gurwitz JH, Yood R. An investigation of the relationship between response rate and patient satisfaction ratings. Society of General Internal Medicine, 22nd Annual Meeting, April 1999.

A48. Donahue J, Andrade S, Beck A, Boles M, Buist D, Chandler J, Chase G, Ettinger B, Goodman M, Guess H, Gurwitz J, Lacroix A, Levin TR, Platt R. Multi-HMO assessment of alendronate and gastro-duodenal perforation, ulcer or bleeding. International Society for Pharmacoeconomics and Outcomes Research 4th Annual International Meeting, May 1999.

A49. Majumdar SR, Inui TS, Gurwitz JH, Gillman MW, McLaughlin TJ, Soumerai SB. Physician specialty and relinquishing calcium channel blockers after acute myocardial infarction. Abstract. J Gen Int Med. 1999; 14 (supplement 2): 108.

A50. Harrold LR, Gurwitz JH, Field TS, Andrade SE, Fish LS, Jarry PD, Yood R. The diffusion of a novel therapy into general medical practice: the case of sildenafil. Fifteenth International Conference on Pharmacoepidemiology, 1999.

A51. Andrade SE, Gurwitz JH, Fish LS, Cernieux J, Yood R. Evaluation of a Comprehensive formulary switch in the managed care setting: the case of hormone replacement therapy. Fifteenth International Conference on Pharmacoepidemiology, 1999.

A52. Field T, Gurwitz J, Avorn J, McCormick D, Jain S, Eckler M, Benser M, Bates DW. Risk factors for adverse drug events among nursing home residents. Fifteenth International Conference on Pharmacoepidemiology, 1999.

A53. Gurwitz J, Field T, Avorn J, McCormick D, Jain S, Eckler M, Benser M, Bates DW. Incidence and preventability of adverse drug events in the nursing home setting. Fifteenth International Conference on Pharmacoepidemiology, 1999.

A54. Harrold L, Yood R, Reed J, Andrade S, Cernieux J, Lewis B, Straus W, Weeks M, Gurwitz JH. Validation of osteoarthritis diagnoses in an administrative database. 63rd Annual Scientific Meeting of the American College of Rheumatology, 1999.

A55. Yood R, Harrold L, Fish L, Cernieux J, Emani S, Conboy B, Gurwitz J. The prevalence of patient education and screening for osteoporosis among patients receiving long-term glucocorticoid therapy. 2000 HMO Research Network Conference.

A56. Field T, Cadoret C, Cernieux J, O'Mara P, Granlund M, Gurwitz J, Silliman R, Prout M, Pransky G, Colton T. Upper body function among breast cancer survivors. 2000 HMO Research Network Conference.

A57. Field T, Gurwitz J, Avorn J, McCormick D, Jain S, Eckler M, Benser M, Bates DW. Risk factors for adverse drug events among nursing home residents. 2000 HMO Research Network Conference.

A58. Gurwitz JH, Guadagnoli E, Silliman R, Weeks J. The treating physician as active gatekeeper in the recruitment of research subjects. 2000 HMO Research Network Conference.

A59. Harrold L, Yood R, Straus W, Andrade S, Reed J, Cernieux J, Lewis B, Weeks M, Gurwitz H. Assessing health care utilization in osteoarthritis: the limitations of identifying a study population solely through administrative data. 2000 HMO Research Network Conference.

A60. Field T, Harrold L, Cadoret C, Granlund M, Gurwitz J, Yood R, Reed J, Lewis B. Use of alternative/complementary medicine among managed care enrollees with osteoarthritis. 2000 HMO Research Network Conference.

A61. Gurwitz J, Gore J, Goldberg R, Barron H, Tiefenbrunn A, Frederick P, Malmgren J. Determinants of hospital transfer in the management of acute myocardial infarction. Society of General Internal Medicine, 23rd Annual Meeting, May 2000.

A62. Harrold LR, Yood RA, Straus W, Andrade SE, Reed JI, Cernieux J, Lewis B, Weeks M, Gurwitz JH. Assessing health care utilization in osteoarthritis: the

limitations of using a population identified solely through administrative data. Society of General Internal Medicine, 23rd Annual Meeting, May 2000.

A63. Soumerai SB, McLaughlin TJ, Ross-Degnan D, Gurwitz JH. Inappropriate use of thrombolytics and excess mortality in the elderly. Society of General Internal Medicine, 23rd Annual Meeting, May 2000.

A64. Field TS, Cadoret CA, Cernieux J, O'Mara P. Granlund M, Gurwitz JH, Silliman R, Prout M, Pransky G, Colton T. Upper body function among breast cancer survivors. Society of General Internal Medicine, 23rd Annual Meeting, May 2000.

A65. Goodman MJ, Gurwitz J, Chan KA, Andrade SE, DeFore TA, Graham D, Platt R. Tramadol and initiation of anticonvulsant therapy. Sixteenth International Conference on Pharmacoepidemiology, 2000, Pharmacoepidemiology and Drug Safety 9(suppl 1):S82.

A66. Chan KA, Donohue JG, Andrade SE, Beck A, Boles M, Buist DSM, Carey VJ, Chandler J, Chase GA, Ettinger B, Fishman P, Goodman M, Guess HA, Gurwitz JH, LaCroix AZ, Levin TR, Platt R. Alendronate, osteoporotic fracture, and gastroduodenal safety. Sixteenth International Conference on Pharmacoepidemiology, 2000, Pharmacoepidemiology and Drug Safety 2000;9(suppl 1):S112.

A67. Field T, Harrold L, Cadoret C, Granlund M, Gurwitz J, Yood R, Reed J, Lewis B, Straus W. Use of alternative/complementary medicine among managed care enrollees with osteoarthritis. 16th International Conference on Epidemiology, 2000, Pharmacoepidemiology and Drug Safety 2000;9(suppl 1):S59.

A68. Gurwitz JH, Andrade S, Cernieux J. Increasing the financial risk of Medicare beneficiaries for drug costs. 53rd Annual Scientific Meeting of the Gerontological Society of America. The Gerontologist 2000;40 (Special Issue I):175.

A69. Yood RA, Harrold LR, Fish L, Cernieux J, Emani S, Conboy E, Gurwitz J. Prevention of glucocorticoid-induced osteoporosis. Arthritis Rheum 2000;43:5142.

A70. Andrade SE, Gurwitz JH. Drug benefit plans under managed care: to what extent do elderly subscribers selecting less drug coverage put themselves at increased financial responsibility? Pharmacoepidemiology and Drug Safety 2001;10 (Suppl 1):S39.

A71. Putnam KG, Chan KA, Fishman PA, Buist DS, Andrade SE, Beck A, Boles M, Goodman MJ, Gurwitz JH, Platt R. Chronic disease score as a predictor of subsequent hospitalization: a multi-HMO study. Pharmacoepidemiology and Drug Safety 2001;10(Suppl 1):S139

A72. Gurwitz JH, Field T, Harrold L, Rothschild J, Debellis K, Seger A, Cadoret C, Fish L, Garber L, Cernieux J, Bates D. The detection of preventable adverse drug events among ambulatory geriatric patients. 2002 Annual Meeting of the American Society for Clinical Pharmacology and Therapeutics.

A73. Malek K, Fink A, Thwin SS, Gurwitz J, Silliman R, Ganz P. Oncologists' and surgeons' perceptions of the risk-benefits of tamoxifen prescription in older breast cancer patients. 2002 Annual Meeting of the American Society of Clinical Oncology.

A74. Field T, Bir A, Cernieux J, Yood R, Gurwitz JH. Capitated Primary Care Physician Compensation: Impact on Care for Enrollees with Diabetes and Hypertension. 2002 HMO Research Network Annual Meeting.

A75. Gurwitz JH, Field T, Harrold L, Rothschild J, Debellis K, Seger A, Cadoret C, Fish L, Garber L, Cernieux J, Bates D. The Detection of Preventable Adverse Drug Events Among Ambulatory Geriatric Patients. 2002 HMO Research Network Annual Meeting.

A76. Harrold L, Yood RA, Bourne L, Walker N, Gurwitz JH. Identifying Patients Interested in a Group Medical Visit Program for the Treatment of Arthritis. 2002 HMO Research Network Annual Meeting.

Annals of Internal Medicine

Exhibit 3
JUN 26 2003

Risk Factors and Secondary Prevention in Women with Heart Disease: The Heart and Estrogen/progestin Replacement Study

Eric Vittinghoff, PhD; Michael G. Shlipak, MD, MPH; Paul D. Varosy, MD; Curt D. Furberg, MD, PhD; Christine C. Ireland, MPH; Steven S. Khan, MD; Roger Blumenthal, MD; Elizabeth Barrett-Connor, MD; and Stephen Hulley, MD, MPH, for the Heart and Estrogen/progestin Replacement Study Research Group

Background: Risk factors for coronary heart disease events have most commonly been evaluated in healthy men.

Objective: To assess risk factors, event rates, and use of secondary prevention treatments in women with preexisting coronary disease.

Design: A prospective cohort of clinical trial participants.

Setting: 20 U.S. clinical centers.

Participants: 2763 postmenopausal women with known coronary disease in the Heart and Estrogen/progestin Replacement Study (HERS).

Measurements: Myocardial infarction or death from coronary heart disease.

Results: On multivariable analysis, the researchers found 11 risk factors: 6 noted by history (nonwhite ethnicity, lack of exercise, treated diabetes, angina, congestive heart failure, and more than one previous myocardial infarction) and 5 that were measured (blood pressure, low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, lipoprotein(a) level, and creatinine clearance). The annual rate of coronary events was 1.3% (95% CI, 0.7% to 2.5%) in women with no risk factors and 8.7% (CI, 7.1% to 10.8%) in women with five or more risk factors (a sixfold increase). At entry into HERS, 83% of participants were receiving aspirin or other antiplatelet agents, 33% were receiving β-blockers, 18% were receiving angiotensin-converting enzyme inhibitors, and 53% were receiving lipid-lowering drugs. Women with more risk factors were less likely to be taking aspirin ($P < 0.001$) and lipid-lowering drugs ($P = 0.006$).

Conclusions: Women with coronary disease are at high risk for myocardial infarction or death from coronary heart disease even in the absence of other risk factors, and their risk increases up to sixfold when many risk factors are present. Established drugs for secondary prevention, including aspirin, β-blockers, and lipid-lowering agents, are underused in these women, especially those at highest risk.

Ann Intern Med. 2003;138:81-89. www.annals.org

For author affiliations, see end of text.

See editorial comment on pp 150-151.

Coronary heart disease (CHD) is the leading cause of death in women. The major independent risk factors that predict CHD onset in healthy women are similar to those identified by epidemiologic studies of healthy men (1–7). A recent report described six independent risk factors—age, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol levels, high blood pressure, diabetes mellitus, and smoking—that were strongly associated with risk for a first CHD event in both men and women (8). However, the strength of the association of certain risk factors with CHD events may vary by sex (9) as well as age. Diabetes may be a stronger risk factor in women than in men (7); among older women, HDL cholesterol level may be a relatively strong risk factor and LDL cholesterol level a relatively weak one (6).

In the period immediately after myocardial infarction (MI), studies of mostly male samples have found that persistent ischemia, impaired left ventricular systolic function, and ventricular arrhythmias are the major determinants of subsequent MI and death (10–13). In the Coronary Drug Project study of men with a history of heart attack, electrocardiographic abnormalities and heart failure were stronger predictors than the atherosclerosis risk factors identified in primary prevention settings (14). However, the risk factors for coronary events among women with recognized but stable coronary disease are mostly unknown. Better understanding of these factors could improve secondary prevention in this large and high-risk group.

The Heart and Estrogen/progestin Replacement Study (HERS) was a randomized clinical trial of estrogen plus progestin for prevention of CHD events in women with coronary disease (15). Overall, no significant differences were noted between the hormone and placebo groups in CHD events; trends of more CHD events with therapy in year 1 were offset by fewer such outcomes during years 4 and 5. The trial collected extensive data on CHD risk factors and medication use and performed exhaustive outcome ascertainment procedures, with complete mortality follow-up. Therefore, HERS offers a unique opportunity to assess the long-term effect of coronary risk factors and use of recommended treatments in women with established coronary disease.

METHODS

Participants

Participants in HERS were postmenopausal women who were younger than 80 years of age, had not had a hysterectomy, and had known coronary artery disease (MI, coronary artery bypass surgery, percutaneous transluminal coronary angioplasty, or angiographic evidence of ≥50% narrowing of one or more major coronary arteries). Women were excluded if they had had a coronary event

© 2003 American College of Physicians–American Society of Internal Medicine

Context

Risk factors for recurrent events among women with known coronary disease and whether these women commonly receive secondary prevention treatments are mostly unknown.

Contribution

This large cohort study showed that 11 different factors, including several previous infarctions, renal dysfunction, diabetes, angina, heart failure, and uncontrolled hypertension, predicted up to a sixfold increased rate of coronary disease events in postmenopausal women with preexisting coronary disease. Despite high risks, half or fewer women were taking β-blockers, angiotensin-converting enzyme inhibitors, or cholesterol-lowering drugs.

Implications

Clinicians can identify women who have high risks for recurrent coronary events and should promote greater use of secondary prevention treatments for them.

–The Editors

within the 6 months before randomization, had a serum triglyceride level greater than 3.39 mmol/L (300 mg/dL), had used hormones within 3 months, or had a history of conditions that would contraindicate estrogen therapy (16). Participants in HERS were randomly assigned within clinical centers to 0.625 mg of conjugated equine estrogen plus 2.5 mg of medroxyprogesterone acetate in one tablet daily (n = 1380) or a placebo of identical appearance (n = 1383). The institutional review boards at the coordinating center and each of the 20 HERS clinical centers approved the protocol, and all participants provided written informed consent.

Predictors

In the baseline interview, information was obtained by self-report on demographic characteristics, behavioral risk factors, and medical history. Among women who reported ever having smoked at least 100 cigarettes, years of smoking, average cigarettes per day, and current smoking were ascertained. Alcohol use in the past 30 days was assessed for frequency and usual numbers of drinks per occasion. Exercise was measured as participation in a "regular exercise program such as cardiac rehabilitation or aerobics" or walking at least occasionally "for exercise more than 10 minutes at a time." Use of aspirin, β-blockers, lipid-lowering medications (statins, niacin, fibrates, bile acid–binding resins, and probucol), angiotensin-converting enzyme (ACE) inhibitors, calcium antagonists, and folate or vitamin B was assessed by self-report.

In the baseline physical examination, blood pressure, waist-to-hip ratio, and body mass index were measured. A physician assessed history and symptoms of heart failure (jugular venous distension, third heart sound, significant murmurs, pulmonary rales, and peripheral edema). High blood pressure was defined as systolic blood pressure greater than or equal to 140 mm Hg or diastolic blood pressure greater than or equal to 90 mm Hg, according to the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (17). Angina was defined as self-report of chest discomfort in the previous 4 weeks during exercise, emotion, or sexual activity. Serum specimens were obtained, and a centralized laboratory measured fasting levels of LDL cholesterol, HDL cholesterol, lipoprotein(a), triglycerides, glucose, and creatinine (15, 16). Creatinine clearance was estimated by using the Cockcroft–Gault equation (18, 19).

Outcomes

The primary HERS outcome was CHD events, defined as nonfatal MI or CHD death. Suspected outcome events were reported within 24 hours to the coordinating center and were systematically assessed every 4 months at the follow-up contacts. An independent morbidity and mortality subcommittee that was blinded to treatment assignment adjudicated all deaths and suspected outcome events. Nonfatal MI was diagnosed by using an algorithm based on ischemic symptoms, electrocardiographic abnormalities, and elevated cardiac enzyme levels (16). Death from CHD included fatal documented MI, sudden death within 1 hour of symptom onset, unobserved death that occurred out of the hospital in the absence of other known causes, or death due to a coronary revascularization procedure or congestive heart failure. The date of each event was determined from the documentation obtained by the clinical centers. The total number of events reported here is slightly larger than that published in the primary HERS results (15) because of subsequent adjudications (20).

Statistical Analyses

We used multivariable Cox proportional hazards models to assess the associations between risk factors and CHD events. These models were stratified by clinical center to account for potential clustering. Waist-to-hip ratio and LDL and HDL cholesterol levels were modeled as continuous variables, but lipoprotein(a) level was dichotomized at the median and creatinine clearance was dichotomized at 0.66 mL/s (40 mL/min) to reflect the nonlinear responses we have reported elsewhere (19, 21). We used an indicator for any alcohol use, since almost all of the 39% of HERS women who reported alcohol use were light or moderate drinkers. Exercise was modeled by an indicator for participation in an exercise program or walking for exercise for more than 10 minutes.

The multivariable model includes previously identified risk factors that were significant ($P \leq 0.20$) in unadjusted models and were not judged redundant on substantive grounds. Body mass index was excluded because it was clearly nonsignificant after adjustment ($P > 0.2$) and was also highly correlated with waist-to-hip ratio, which was

the stronger predictor in unadjusted analysis. Similarly, triglyceride levels were excluded because of their strong negative correlation with HDL cholesterol levels, which in our judgment were more likely to be causal. We also controlled for use of aspirin, statins, other lipid-lowering medications, diuretics, β-blockers, ACE inhibitors, calcium antagonists, and folate or vitamin B. The effect of assignment to hormone therapy was modeled separately for each year of follow-up, as in the post hoc analysis of HERS (15).

Interactions between risk factors and relevant treatments were also examined. Specifically, we compared hazard rates among patients with diagnosed diabetes who reported use of insulin or oral hypoglycemic agents with rates in the combined group of diabetic persons not using these medications and women with fasting glucose levels greater than 6.94 mmol/L (>125 mg/dL) but no history of diabetes diagnosis. Likewise, we compared estimates for LDL and HDL cholesterol levels stratified by use of any lipid-lowering medication or assignment to hormone therapy; for lipoprotein(a) level, stratified by assignment to hormone therapy; for high blood pressure on examination, stratified by use of at least one antihypertensive medication; for heart failure and creatinine clearance less than or equal to 0.66 mL/s (≤40 mL/min), stratified by use of ACE inhibitors; and for more than one previous MI and angina, stratified by use of any indicated medications. The final model includes interactions that were significant at a P value less than or equal to 0.2.

We used residuals to assess overall model fit, validity of the proportional hazards assumption, and linearity of associations with continuous predictors. The study lacked power to examine interactions between clinical center and potential risk factors. We tested the assumption of noninformative censoring by considering the two extremes of the possible outcomes for the 60 women lost to clinical follow-up before the end of HERS, first as events at the time of censoring, then as observations censored at the longest observed follow-up time.

The average annual rate of CHD events was estimated overall and for groups defined by number of risk factors present among the 11 predictors identified in the multivariable Cox model. To evaluate this number, LDL and HDL cholesterol levels were dichotomized at standard cutpoints for elevated risk. Within these groups, we tabulated use of aspirin and other antiplatelet agents, β-blockers, ACE inhibitors, and lipid-lowering therapy, both at baseline and at the end of the study. We also tabulated the proportions of women with various risk factors who were receiving indicated treatments. Because the third report of the National Cholesterol Education Program has only recently been published (22), the denominator for lipid-lowering medication use excluded nonusers with LDL cholesterol levels less than 3.4 mmol/L (<130 mg/dL), which was the criterion for initiating therapy among women with coronary disease in the second report of the National Cholesterol Education Program (NCEP II) (23). Similarly, the denominator for use of aspirin or other antiplatelet agents excluded women using warfarin. All analyses were performed by using SAS, version 8.02 (SAS Institute, Inc., Cary, North Carolina).

Role of the Funding Source

Wyeth-Ayerst Research funded the HERS clinical trial, implemented data collection, and reviewed the manuscript before submission for publication. The investigators were not required by contract to make any revisions suggested by Wyeth-Ayerst.

RESULTS

During an average of 4.1 years of follow-up in 1993 to 1998, 361 of 2763 women in HERS had nonfatal MI or died of CHD. Of the 232 women with nonfatal MI, 24 subsequently died of CHD. The 129 CHD deaths included 35 fatal MIs, 38 sudden deaths, 16 deaths from congestive heart failure or pulmonary edema, 24 deaths that were unwitnessed or occurred during sleep, and 16 deaths from other or unclassified CHD causes.

Unadjusted Analyses

Nonwhite women were twice as likely as white women to have a CHD event (**Table 1**). Both alcohol use and regular exercise were associated with lower event rates. Treated diabetes, congestive heart failure, a history of at least two MIs, and angina by self-report were associated with increased event rates. Higher blood pressure, waist-to-hip ratio, LDL cholesterol level, and triglyceride levels, as well as lower HDL cholesterol level and creatinine clearance (≤0.66 mL/s [≤40 mL/min]) were associated with CHD events.

Adjusted Analyses

In the multivariable model (**Table 2**), increased rates of CHD events were associated with diabetes (among those taking insulin or oral hypoglycemic agents), high blood pressure, at least two previous MIs, heart failure, angina, creatinine clearance less than or equal to 0.66 mL/s (≤40 mL/min), lipoprotein(a) level at least 0.90 mmol/L (≥25.3 mg/dL) among women assigned to placebo, lack of exercise, and African-American ethnicity. We also found probable associations with higher LDL and lower HDL cholesterol levels (P = 0.06 for both). Weaker evidence was observed for increased rates among Latin-American women and women of other nonwhite ethnicity, older women, and current smokers. The findings were similar if weak predictors (including former smoking, untreated diabetes, lipoprotein(a) level among women assigned to hormone therapy, and previous percutaneous transluminal coronary angioplasty) were excluded from the model, or if we used a quantitative measure of alcohol use. The estimate for HDL cholesterol level was attenuated if triglyceride level was added to the model shown in **Table 2**, but triglyceride level is the weaker predictor and was nonsignificant. Furthermore, triglyceride level was not statistically significant in a

Table 1. **Risk Factors for Coronary Heart Disease Events***

Risk Factor	Participants without CHD Events (n = 2402)	Participants with CHD Events (n = 361)	Relative Hazard (95% CI)†	P Value
Demographic characteristics				
Mean age at randomization ± SD, *y*	66.6 ± 6.6	66.9 ± 6.7	1.11 (0.95–1.30)	0.2
Ethnicity, %				
African American	7	14	2.05 (1.52–2.77)	<0.001
Latin American	2	3	1.61 (0.86–3.03)	0.14
Other nonwhite	1	2	1.87 (0.93–3.78)	0.08
Health-related behaviors, %				
Smoking				
Current	13	15	1.24 (0.93–1.65)	0.14
Former	50	44	0.84 (0.67–1.06)	0.14
Any alcohol consumption	40	31	0.67 (0.53–0.83)	<0.001
Exercise‡	66	53	0.60 (0.49–0.74)	<0.001
Medical conditions, %§				
Diabetes				
Receiving insulin or oral hypoglycemic agents	17	29	2.01 (1.59–2.54)	<0.001
Other	8	8	1.12 (0.76–1.66)	>0.2
≥2 previous myocardial infarctions	5	9	1.88 (1.30–2.72)	<0.001
Previous PTCA	44	40	0.85 (0.69–1.05)	0.14
Angina	25	36	1.66 (1.34–2.05)	<0.001
Physical examination				
Mean BMI ± SD, kg/m^2	28.5 ± 5.4	29.1 ± 6.1	1.09 (0.98–1.20)	0.10
Mean waist-to-hip ratio ± SD	0.87 ± 0.08	0.88 ± 0.08	1.15 (1.04–1.28)	0.007
High blood pressure, %‖	37	49	1.61 (1.31–1.98)	<0.001
History or symptoms of CHF, %	11	19	1.76 (1.35–2.28)	<0.001
Laboratory results				
Mean LDL cholesterol level ± SD, *mmol/L (mg/dL)*	3.74 ± 0.97 (144 ± 38)	3.90 ± 1.02 (151 ± 40)	1.15 (1.05–1.27)	0.004
Mean HDL cholesterol level ± SD, *mmol/L (mg/dL)*	1.31 ± 0.34 (50.6 ± 13.3)	1.25 ± 0.32 (48.3 ± 12.4)	0.85 (0.76–0.95)	0.004
Lipoprotein(a) level > 0.90 mmol/L (>25.3 mg/dL), %				
Placebo group	24	30	1.49 (1.11–2.00)	0.008
Hormone therapy group	25	25	0.97 (0.72–1.30)	>0.2
Mean triglyceride level ± SD, *mmol/L (mg/dL)*	1.87 ± 0.71 (165 ± 63)	1.96 ± 0.75 (173 ± 66)	1.14 (1.03–1.26)	0.01
Creatinine clearance ≤ 0.66 mL/s (≤40 mL/min), %	11	17	1.78 (1.35–2.34)	<0.001

* Coronary heart disease events include nonfatal myocardial infarction and death from CHD. All listed risk factors were previously identified as associated with CHD events in unadjusted analysis ($P \leq 0.20$). Additional variables screened in preliminary analysis include education, marital status, living situation, heart rate, and individual signs of heart failure. BMI = body mass index; CHD = coronary heart disease; CHF = congestive heart failure; HDL = high-density lipoprotein; LDL = low-density lipoprotein; PTCA = percutaneous transluminal coronary angioplasty.

† From unadjusted Cox models. The relative hazard is per 10 years for age and per SD for BMI; waist-to-hip ratio; and LDL cholesterol, HDL cholesterol, and triglyceride levels.

‡ Defined as regular participation in an exercise program or walking for at least 10 minutes.

§ Other women with diabetes include those reporting a history of diagnosis but no medication use and women with fasting plasma glucose levels > 6.94 mmol/L (>125 mg/dL). Angina was defined by self-report as chest pain in the past 4 weeks during exercise, emotion, or sexual activity.

‖ High blood pressure is defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥90 mm Hg.

multivariable model from which HDL level was excluded. The multivariable model was determined by using data for 2740 of 2763 women (99%) with no missing covariate values and included 354 of the 361 observed events (98%). We found little evidence for violation of the proportional hazards assumption ($P > 0.2$). However, the results for HDL cholesterol level and smoking were uncertain because they were sensitive to the untestable assumption of noninformative censoring.

CHD Events and Use of Medications by Number of Risk Factors

Overall, the average annual rate of CHD events was 3.4% (95% CI, 3.1% to 3.8%) (Table 3). Half of all women had at least two risk factors. Average annual rates increased sixfold, from 1.3% among women with no risk factors to 8.7% among women with five or more risk factors ($P < 0.001$ for trend). Despite this increasing gradient, women with five or more risk factors appeared to be the least likely to receive aspirin ($P < 0.001$ for trend) and lipid-lowering therapy ($P = 0.006$ for trend). Use of β-blockers was similar across subgroups. Use of ACE inhibitors, however, increased with the number of risk factors ($P < 0.001$ for trend).

Time Trends in Secondary Prevention

We also examined use of these secondary prevention drugs at the end of the study. Use of aspirin and other antiplatelet agents had decreased slightly from 83% to 79%, and use of β-blockers was essentially unchanged (33% vs. 35%) (Table 3). Use of any lipid-lowering medication had increased from 53% to 66% among women who met NCEP II criteria; most were taking statins. The associations at baseline between number of risk factors and use of aspirin or other antiplatelet agents, ACE inhibitors, and lipid-lowering therapy persisted at the end of the study.

Use of Indicated Medications by Risk Factor

For certain risk factors, we evaluated the proportions of women using indicated medications. Only 37% of women with diagnosed heart failure and only 24% of women with creatinine clearance of 0.66 mL/s or less (≤40 mL/min) used ACE inhibitors (**Table 4**). Use of β-blockers and aspirin or other antiplatelet agents was similar among women with previous MI and those with angina symptoms.

Discussion

We found 11 risk factors for MI or coronary death in our cohort of women with previous coronary artery disease. Of these factors, 6 were noted by history (nonwhite ethnicity, lack of exercise, treated diabetes, angina, congestive heart failure, and more than one previous MI) and 5 were measured (blood pressure, LDL cholesterol level, HDL cholesterol level, lipoprotein(a) level, and creatinine clearance). Compared with women in primary prevention settings (8), women with no risk factors had a substantial absolute risk for nonfatal MI or CHD death. This risk was increased sixfold in women with five or more risk factors.

Two of the six conventional risk factors that were independent predictors of CHD events in healthy middle-aged women in the Framingham Study (8) were not risk factors in HERS. The nonsignificant relative hazard estimates for age and smoking in our study appear to differ from findings in other samples of persons with coronary disease (14, 24), but wide confidence intervals suggest that the differences between studies would not be statistically significant. In addition, because smoking was not prevalent in HERS, we had less power to detect a clinically relevant association. The relative hazards for diabetes, high blood pressure, LDL cholesterol level, and HDL cholesterol level in women in HERS, while statistically significant, were somewhat weaker than those estimated in women without CHD (6, 8) and resemble findings in men with previous coronary disease (14). The excess event rates associated with these risk factors are greater than in primary prevention because the baseline rate in the secondary prevention setting is substantially higher (25).

Differing patterns of risk factors in HERS compared with primary prevention settings may result from differences in age or in the presence of established coronary disease. Participants in HERS were on average 67 years of age, and some risk factors, notably serum cholesterol level and tobacco use, may become less predictive of CHD events as age increases (26, 27). In addition, determinants of atherosclerosis, which play a central role in predicting CHD risk in patients without manifest coronary disease, may be less important than measures of recurrent ischemia, myocardial function, and arrhythmia in patients in whom coronary disease has been established (10–13, 28).

Although all participants in HERS had established coronary artery disease, only about half had had an MI before enrollment. Twenty-six percent reported angina, and 12% had had heart failure. We found that those with two or more previous MIs and those with angina had substantially greater risk for subsequent CHD events. Congestive heart failure was also independently associated with CHD events. Because women with severe symptoms of heart failure were excluded from HERS, we may have underestimated the association of heart failure with coronary events in women with known coronary disease.

Table 2. **Multivariate Cox Regression Analyses of Risk Factors for Coronary Heart Disease Events***

Risk Factor	Relative Hazard (95% CI)	P Value
Well supported by overall evidence, including previous findings		
Ethnicity		
African American	1.44 (1.02–2.04)	0.04
Latin American	1.92 (0.95–3.91)	0.07
Other nonwhite	1.87 (0.89–3.91)	0.10
Exercise program or walking for ≥10 minutes	0.80 (0.64–1.00)	0.05
High blood pressure on examination†	1.55 (1.16–2.07)	0.003
Diabetes treated with insulin or oral hypoglycemic agents‡	1.51 (1.16–1.98)	0.001
LDL cholesterol level (per SD)	1.10 (1.00–1.22)	0.06
HDL cholesterol level (per SD)	0.89 (0.79–1.01)	0.06
Lipoprotein(a) level > 0.90 mmol/L (>25.3 mg/dL) in the placebo group§	1.44 (1.06–1.96)	0.02
Creatinine clearance ≤ 0.66 mL/s (≤40 mL/min)	1.56 (1.16–2.11)	0.004
≥2 previous myocardial infarctions	1.79 (1.22–2.62)	0.003
History or symptoms of CHF	1.33 (1.00–1.78)	0.05
Angina‖	1.49 (1.18–1.87)	<0.001
Other		
Age (per 10 years)	1.13 (0.94–1.37)	0.19
Smoking		
Current	1.30 (0.92–1.84)	0.13
Past	0.99 (0.78–1.26)	>0.2
Any alcohol use	0.97 (0.75–1.25)	>0.2
Waist-to-hip ratio (per 0.10 unit)	1.03 (0.89–1.20)	>0.2
Other diabetes¶	0.91 (0.60–1.36)	>0.2
History of hypertension with normal blood pressure	1.18 (0.87–1.62)	>0.2
Lipoprotein(a) level > 0.90 mmol/L (>25.3 mg/dL) in the hormone therapy group**	0.97 (0.71–1.32)	>0.2
Previous PTCA	0.94 (0.76–1.18)	>0.2

* Coronary heart disease events include nonfatal myocardial infarction and death from coronary heart disease. Estimates are adjusted for assignment to hormone therapy and for use of statins, other lipid-lowering medications, aspirin, angiotensin-converting enzyme inhibitors, β-blockers, calcium antagonists, diuretics, and folate or vitamin B. The factors in Table 1 were considered for inclusion in the multivariable model; only body mass index and triglyceride level were excluded (see Methods). CHF = congestive heart failure; HDL = high-density lipoprotein; LDL = low-density lipoprotein; PTCA = percutaneous coronary angioplasty.

† High blood pressure is defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥90 mm Hg.

‡ The reference group is women who did not report a history of diagnosis and had a baseline glucose level ≤ 6.94 mmol/L (≤125 mg/dL).

§ The reference group is women assigned to placebo who had a lipoprotein(a) level ≤ 0.90 mmol/L (≤25.3 mg/dL).

‖ Angina is defined by self-report as chest pain in the past 4 weeks during exercise, emotion, or sexual activity.

¶ Includes women reporting a history of diagnosis but no medication use and those with fasting plasma glucose levels > 6.94 mmol/L (>125 mg/dL). The reference group is women who did not report a history of diagnosis and had a baseline glucose level ≤ 6.94 mmol/L (≤125 mg/dL).

** The reference group is women assigned to hormone therapy who had a lipoprotein(a) level at or below the median.

Table 3. **Risk for Coronary Heart Disease Events and Use of Preventive Medications according to Number of Risk Factors***

Risk Factors†	Women	Annual CHD Event (95% CI)‡	Women Taking Aspirin and Other Antiplatelet Agents§		Women Taking β-Blockers		Women Taking ACE Inhibitors		Women Taking Lipid-Lowering Drugs‖	
			Baseline	End of the Study	Baseline	End of the Study	Baseline	End of the Study	Baseline	End of the Study
	n (%)		%							
0	164 (6)	1.3 (0.7–2.5)	94	85	36	35	10	12	58	72
1	540 (20)	2.4 (1.9–3.2)	89	82	30	35	12	22	53	68
2	722 (26)	2.1 (1.7–2.7)	84	80	31	34	15	23	54	62
3	656 (24)	3.3 (2.6–4.1)	82	77	32	36	17	28	51	62
4	398 (14)	5.1 (4.1–6.4)	80	78	34	33	21	32	45	55
≥5	283 (10)	8.7 (7.1–10.8)	77	76	37	37	29	42	48	59
Overall	2763 (100)	3.4 (3.1–3.8)	83	79	33	35	18	28	53	66

* *P* value for trend in risk by number of risk factors is <0.001. ACE = angiotensin-converting enzyme; CHD = coronary heart disease.
† Number of risk factors includes lack of exercise, systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, diabetes, low-density lipoprotein cholesterol level > 3.4 mmol/L (>130 mg/dL), high-density lipoprotein cholesterol level < 0.91 mmol/L (<35 mg/dL), lipoprotein(a) level > 0.90 mmol/L (>25.3 mg/dL), nonwhite ethnicity, creatinine clearance ≤ 0.66 mL/s (≤40 mL/min), ≥2 previous myocardial infarctions, angina, and heart failure. These are the 11 risk factors identified as important in the multivariable model (Table 2). To evaluate the number of risk factors, low-density lipoprotein cholesterol level and high-density lipoprotein cholesterol level were dichotomized at established cut-points for elevated CHD risk.
‡ 95% CIs were computed under a Poisson assumption.
§ For aspirin and antiplatelet agents, the denominators excluded women using warfarin.
‖ For lipid-lowering medications, the number of risk factors does not include levels of low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, or lipoprotein(a). Denominators excluded nonusers with normal lipid levels.

Whereas symptoms of angina and heart failure were associated with increased event rates, regular exercise was associated with decreased CHD events in HERS. This finding could represent the benefits of physical activity among women with CHD or simply reflect the greater propensity of healthy women to exercise. In contrast, we did not find obesity, defined either by body mass index or waist-to-hip ratio, to be a significant independent risk factor in HERS after adjustment for exercise and other covariates. However, because of the significant unadjusted association between obesity and CHD events and because it is a modifiable risk factor for high blood pressure and diabetes, obesity is an appropriate target for secondary prevention efforts (29).

We identified two risk factors in HERS that are not as well known: reduced renal function and elevated lipoprotein(a) levels. Moderate renal insufficiency has been increasingly recognized as an independent predictor of cardiovascular events and death, but the mechanisms for the association are not clear (6, 21, 30, 31). Renal insufficiency has been linked both to the incidence of heart failure and to poor survival after heart failure (32, 33). Prevalence of moderate renal insufficiency, as defined by estimated creatinine clearance less than or equal to 0.66 mL/s (≤40

Table 4. **Use of Indicated Medications by Risk Factor Status***

Risk Factor	Indicated Medication	All Women with the Risk Factor	Women with the Risk Factor Who Were Receiving the Indicated Medication
		n (%)	
LDL cholesterol level ≥ 3.4 mmol/L (≥130 mg/dL)	Any lipid-lowering therapy	2355 (85)†	1287 (55)
	Statins		1004 (43)
History or symptoms of CHF	ACE inhibitors	345 (12)	128 (37)
Any previous MI	β-blockers	1409 (51)	477 (34)
	Aspirin or other antiplatelet agent		1134 (80)
≥2 previous MIs	β-blockers	143 (5)	44 (31)
	Aspirin or other antiplatelet agent		109 (76)
Angina without history of MI	β-blockers	383 (14)	157 (41)
	Aspirin or other antiplatelet agent		298 (78)
Creatinine clearance ≤ 0.66 mL/s (≤40 mL/min)	ACE inhibitors	323 (12)	78 (24)

* ACE = angiotensin-converting enzyme; CHF = congestive heart failure; HDL = high-density lipoprotein; LDL = low-density lipoprotein; MI = myocardial infarction.
† Includes women with normal LDL cholesterol level who were receiving lipid-lowering therapy.

mL/min), was 13% in the HERS cohort. This prevalence increases with age, making moderate renal insufficiency a risk factor of greater importance in this sample than in younger women (19).

Lipoprotein(a) levels were also a statistically significant risk factor, but only in the placebo group. The absence of an association between lipoprotein(a) level and CHD events in the active treatment group can probably be explained by the reduction in lipoprotein(a) levels caused by hormone therapy. We have previously shown that for women in HERS, reductions in lipoprotein(a) levels were independently associated with reduced rates of CHD events (21). Lipoprotein(a) level may prove to be an important consideration in secondary prevention efforts.

Despite the high CHD risk among HERS participants, the use of medications for secondary prevention was inadequate. In women with heart disease, treatment with aspirin, β-blockers, and lipid-lowering agents is one of the cornerstones of secondary prevention (22, 29, 34). One of the most important findings in HERS was the substantial underuse of these proven therapies (35, 36). Although most women in HERS were taking aspirin at enrollment, only one third were treated with β-blockers and only half of those who met NCEP II criteria for lipid-lowering therapy were using statins or other lipid-lowering treatments. Of concern, the women who had the greatest risk for CHD events in HERS were the least likely to be treated with aspirin or lipid-lowering medications. Furthermore, during the 4-year follow-up, use of β-blockers remained unchanged and use of aspirin and other antiplatelet agents decreased. Although use of statins increased during HERS, only two thirds of participants who met 1993 NCEP II criteria for treatment were taking lipid-lowering agents at the end of the study. Similarly low rates of utilization of these medications, as well as of other preventive interventions (ACE inhibitors, blood pressure and weight control, diet, exercise, and smoking cessation), have been observed in other clinical settings (37–44). In addition, women often receive less treatment than men (45–47). Proactive, targeted interventions should be developed to improve utilization of these preventive therapies (48).

The primary limitation of our study is that we examined voluntary participants in a secondary prevention trial. Our sample therefore may differ from the general population of women with coronary artery disease. Clinical trial participants tend to be healthier and more health conscious and therefore may be less in need of and more likely to engage in preventive behaviors. In addition, the enrollment criteria for HERS excluded the most infirm candidates, as evidenced by the lower-than-expected event rates (15). As a result, the significant associations we detected with dichotomous risk factors, including hypertension, diabetes, heart failure, and renal insufficiency, could represent underestimates. However, only 6% of women screened were excluded because of high serum levels of triglycerides, aspartate aminotransferase, or glucose (16).

The risk factor classifications that we considered important were to some extent data driven. This may inflate the type I error rates or the likelihood of mistakenly concluding that the observed associations are important. Our conclusion that LDL and HDL cholesterol levels are important risk factors was based on our interpretation of a multivariate P value of 0.06 in the context of information from other studies; other interpretations may also be valid. A further limitation is that the predictor variables measured in HERS did not include diagnostic tests, such as echocardiography and exercise testing, that might better predict clinical outcomes among women with coronary artery disease than risk factors for atherosclerosis. We also did not have good information on contraindications to medications, which may mean that our estimates of appropriate utilization are too low.

In conclusion, we used multivariable analysis to identify 11 easily assessed characteristics that predicted up to a sixfold increase in CHD events in a large sample of women who were already at high risk because they had coronary disease. This set of risk factors differs from those that have been established in primary prevention settings. In addition, we found substantial underuse of preventive treatments that have been established as beneficial, notably aspirin, β-blockers, and statins.

From the University of California, San Francisco, and Veterans Affairs Medical Center, San Francisco, California; Wake Forest University School of Medicine, Winston-Salem, North Carolina; University of California, Los Angeles, Los Angeles, California; Johns Hopkins University, Baltimore, Maryland; and University of California, San Diego, San Diego, California.

Grant Support: By Wyeth-Ayerst Laboratories. Dr. Shlipak is funded by a Research Career Development Award from the Health Services Research and Development Service of the Veterans Affairs Administration.

Potential Financial Conflicts of Interest: *Consultancies:* C.D. Furberg; *Honoraria:* M.G. Shlipak, C.D. Furberg, S.S. Khan; *Grants received:* E. Vittinghoff, M.G. Shlipak, C.D. Furberg, C.C. Ireland, S.S. Khan, R. Blumenthal, E. Barrett-Connor, S. Hulley.

Requests for Single Reprints: Eric Vittinghoff, PhD, University of California, San Francisco, 74 New Montgomery, Suite 600, San Francisco, CA 94105.

Current author addresses and author contributions are available at www.annals.org.

References

1. Mosca L, Manson JE, Sutherland SE, Langer RD, Manolio T, Barrett-Connor E. Cardiovascular disease in women: a statement for healthcare professionals from the American Heart Association. Writing Group. Circulation. 1997; 96:2468-82. [PMID: 9337227]

2. Grundy SM, Balady GJ, Criqui MH, Fletcher G, Greenland P, Hiratzka LF, et al. Primary prevention of coronary heart disease: guidance from Framingham: a statement for healthcare professionals from the AHA Task Force on Risk Reduction. American Heart Association. Circulation. 1998;97:1876-87. [PMID: 9603549]

3. Denke MA. Primary prevention of coronary heart disease in postmenopausal women. Am J Med. 1999;107:48S-50S. [PMID: 10484243]

4. Willett WC, Green A, Stampfer MJ, Speizer FE, Colditz GA, Rosner B, et al. Relative and absolute excess risks of coronary heart disease among women who smoke cigarettes. N Engl J Med. 1987;317:1303-9. [PMID: 3683458]

5. Kannel WB, Higgins M. Smoking and hypertension as predictors of cardiovascular risk in population studies. J Hypertens Suppl. 1990;8:S3-8. [PMID: 2286855]

6. Manolio TA, Pearson TA, Wenger NK, Barrett-Connor E, Payne GH, Harlan WR. Cholesterol and heart disease in older persons and women. Review of an NHLBI workshop. Ann Epidemiol. 1992;2:161-76. [PMID: 1342259]

7. Barrett-Connor E. Sex differences in coronary heart disease. Why are women so superior? The 1995 Ancel Keys Lecture. Circulation. 1997;95:252-64. [PMID: 8994444]

8. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation. 1998;97:1837-47. [PMID: 9603539]

9. Manson JE. Prevention of Myocardial Infarction. New York: Oxford Univ Pr; 1996.

10. Moss AJ, DeCamilla JJ, Davis HP, Bayer L. Clinical significance of ventricular ectopic beats in the early posthospital phase of myocardial infarction. Am J Cardiol. 1977;39:635-40. [PMID: 67792]

11. Henning H, Gilpin EA, Covell JW, Swan EA, O'Rourke RA, Ross J Jr. Prognosis after acute myocardial infarction: a multivariate analysis of mortality and survival. Circulation. 1979;59:1124-36. [PMID: 436204]

12. Epstein SE, Palmeri ST, Patterson RE. Current concepts: evaluation of patients after acute myocardial infarction: indications for cardiac catheterization and surgical intervention. N Engl J Med. 1982;307:1487-92. [PMID: 6755248]

13. O'Rourke RA. Risk stratification after myocardial infarction. Clinical overview. Circulation. 1991;84:I177-81. [PMID: 1884483]

14. Schlant RC, Forman S, Stamler J, Canner PL. The natural history of coronary heart disease: prognostic factors after recovery from myocardial infarction in 2789 men. The 5-year findings of the coronary drug project. Circulation. 1982;66:401-14. [PMID: 7094247]

15. Hulley S, Grady D, Bush T, Furberg C, Herrington D, Riggs B, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group. JAMA. 1998;280:605-13. [PMID: 9718051]

16. Grady D, Applegate W, Bush T, Furberg C, Riggs B, Hulley SB. Heart and Estrogen/progestin Replacement Study (HERS): design, methods, and baseline characteristics. Control Clin Trials. 1998;19:314-35. [PMID: 9683309]

17. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Arch Intern Med. 1997;157:2413-46. [PMID: 9385294]

18. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16:31-41. [PMID: 1244564]

19. Shlipak MG, Simon JA, Grady D, Lin F, Wenger NK, Furberg CD, et al. Renal insufficiency and cardiovascular events in postmenopausal women with coronary heart disease. J Am Coll Cardiol. 2001;38:705-11. [PMID: 11527621]

20. Hulley SB, Grady D, Vittinghoff E, Bush T, Furberg C, Herrington D, et al. Hormone replacement therapy for secondary prevention of coronary heart disease [Letter]. JAMA. 1999;281:796-7.

21. Shlipak MG, Simon JA, Vittinghoff E, Lin F, Barrett-Connor E, Knopp RH, et al. Estrogen and progestin, lipoprotein(a), and the risk of recurrent coronary heart disease events after menopause. JAMA. 2000;283:1845-52. [PMID: 10770146]

22. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA. 2001;285:2486-97. [PMID: 11368702]

23. Summary of the second report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). JAMA. 1993;269:3015-23. [PMID: 8501844]

24. Vaccarino V, Krumholz HM, Yarzebski J, Gore JM, Goldberg RJ. Sex differences in 2-year mortality after hospital discharge for myocardial infarction. Ann Intern Med. 2001;134:173-81. [PMID: 11177329]

25. Siegel D, Grady D, Browner WS, Hulley SB. Risk factor modification after myocardial infarction. Ann Intern Med. 1988;109:213-8. [PMID: 3291658]

26. Kronmal RA, Cain KC, Ye Z, Omenn GS. Total serum cholesterol levels and mortality risk as a function of age. A report based on the Framingham data. Arch Intern Med. 1993;153:1065-73. [PMID: 8481074]

27. Psaty BM, Furberg CD, Kuller LH, Bild DE, Rautaharju PM, Polak JF, et al. Traditional risk factors and subclinical disease measures as predictors of first myocardial infarction in older adults: the Cardiovascular Health Study. Arch Intern Med. 1999;159:1339-47. [PMID: 10386510]

28. Factors influencing long-term prognosis after recovery from myocardial infarction—three-year findings of the coronary drug project. J Chronic Dis. 1974;27:267-85. [PMID: 4610000]

29. Gibbons RJ, Chatterjee K, Daley J, Douglas JS, Fihn SD, Gardin JM, et al. ACC/AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Chronic Stable Angina). J Am Coll Cardiol. 1999;33:2092-197. [PMID: 10362225]

30. Shulman NB, Ford CE, Hall WD, Blaufox MD, Simon D, Langford HG, et al. Prognostic value of serum creatinine and effect of treatment of hypertension on renal function. Results from the hypertension detection and follow-up program. The Hypertension Detection and Follow-up Program Cooperative Group. Hypertension. 1989;13:180-93. [PMID: 2490833]

31. Mann JF, Gerstein HC, Pogue J, Bosch J, Yusuf S. Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: the HOPE randomized trial. Ann Intern Med. 2001;134:629-36. [PMID: 11304102]

32. Gottdiener JS, Arnold AM, Aurigemma GP, Polak JF, Tracy RP, Kitzman DW, et al. Predictors of congestive heart failure in the elderly: the Cardiovascular Health Study. J Am Coll Cardiol. 2000;35:1628-37. [PMID: 10807470]

33. Dries DL, Exner DV, Domanski MJ, Greenberg B, Stevenson LW. The prognostic implications of renal insufficiency in asymptomatic and symptomatic patients with left ventricular systolic dysfunction. J Am Coll Cardiol. 2000;35:681-9. [PMID: 10716471]

34. Ryan TJ, Antman EM, Brooks NH, Califf RM, Hillis LD, Hiratzka LF, et al. 1999 update: ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction: Executive Summary and Recommendations: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). Circulation. 1999;100:1016-30. [PMID: 10468535]

35. Schrott HG, Bittner V, Vittinghoff E, Herrington DM, Hulley S. Adherence to National Cholesterol Education Program Treatment goals in postmenopausal women with heart disease. The Heart and Estrogen/Progestin Replacement Study (HERS). The HERS Research Group. JAMA. 1997;277:1281-6. [PMID: 9109465]

36. Herrington DM, Fong J, Sempos CT, Black DM, Schrott HG, Rautaharju P, et al. Comparison of the Heart and Estrogen/Progestin Replacement Study (HERS) cohort with women with coronary disease from the National Health and Nutrition Examination Survey III (NHANES III). Am Heart J. 1998;136:115-24. [PMID: 9665228]

37. Hulley SB, Grady D, Browner WS. Statins: underused by those who would benefit [Editorial]. BMJ. 2000;321:971-2. [PMID: 11039939]

38. Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I and II in nine countries. EUROASPIRE I and II Group. European Action on Secondary Prevention by Intervention to Reduce Events. Lancet. 2001;357:995-1001. [PMID: 11293642]

39. Allen JK, Blumenthal RS, Margolis S, Young DR. Status of secondary prevention in patients undergoing coronary revascularization. Am J Cardiol. 2001;87:1203-6: A7. [PMID: 11356400]

40. McCormick D, Gurwitz JH, Lessard D, Yarzebski J, Gore JM, Goldberg RJ. Use of aspirin, beta-blockers, and lipid-lowering medications before recurrent acute myocardial infarction: missed opportunities for prevention? Arch Intern Med. 1999;159:561-7. [PMID: 10090112]

41. Giugliano RP, Camargo CA Jr, Lloyd-Jones DM, Zagrodsky JD, Alexis JD, Eagle KA, et al. Elderly patients receive less aggressive medical and invasive management of unstable angina: potential impact of practice guidelines. Arch Intern Med. 1998;158:1113-20. [PMID: 9605783]

42. Gottlieb SS, McCarter RJ, Vogel RA. Effect of beta-blockade on mortality among high-risk and low-risk patients after myocardial infarction. N Engl J Med. 1998;339:489-97. [PMID: 9709041]

43. Wang TJ, Stafford RS. National patterns and predictors of beta-blocker use in patients with coronary artery disease. Arch Intern Med. 1998;158:1901-6. [PMID: 9759686]

44. Krumholz HM, Radford MJ, Wang Y, Chen J, Heiat A, Marciniak TA. National use and effectiveness of beta-blockers for the treatment of elderly patients after acute myocardial infarction: National Cooperative Cardiovascular Project. JAMA. 1998;280:623-9. [PMID: 9718054]

45. Clarke KW, Gray D, Keating NA, Hampton JR. Do women with acute myocardial infarction receive the same treatment as men? BMJ. 1994;309:563-6. [PMID: 7916228]

46. Schwartz LM, Fisher ES, Tosteson NA, Woloshin S, Chang CH, Virnig BA, et al. Treatment and health outcomes of women and men in a cohort with coronary artery disease. Arch Intern Med. 1997;157:1545-51. [PMID: 9236556]

47. Alexander KP, Peterson ED, Granger CB, Casas AC, Van de Werf F, Armstrong PW, et al. Potential impact of evidence-based medicine in acute coronary syndromes: insights from GUSTO-IIb. Global Use of Strategies to Open Occluded Arteries in Acute Coronary Syndromes trial. J Am Coll Cardiol. 1998;32:2023-30. [PMID: 9857888]

48. Fonarow GC, Gawlinski A, Moughrabi S, Tillisch JH. Improved treatment of coronary heart disease by implementation of a Cardiac Hospitalization Atherosclerosis Management Program (CHAMP). Am J Cardiol. 2001;87:819-22. [PMID: 11274933]

AD LIBITUM

Sunday at the Nursing Home

My mother is shrinking.
When I was little she was huge,
a mountain of a woman,
her peak covered by clouds of curls.
I craned my neck to the skies
just to see her smile.
Getting dressed, naked,
putting on her bra, she loomed:
Enormous. Majestic.
Now she is mostly flat, lying
on strange sheets:
More a prairie with dried grass
I flex my neck down to view.
My little boy watches me, too.
It's impossible not to notice
everyday
I get
smaller.

Bonnie Salomon, MD
Lake Forest, IL 60045

Current Author Address: Bonnie Salomon, MD, Emergency Department, Lake Forest Hospital, 660 North Westmoreland, Lake Forest, IL 60045.

Exhibit 9

Secondary Prevention of Coronary Heart Disease in Women: A Call to Action

On the basis of extensive mechanistic evidence from in vitro and animal studies and clinical evidence from observational studies, it was predicted that postmenopausal hormone replacement therapy would protect women from coronary heart disease (CHD) events. However, the results of randomized, controlled trials available to date have not supported this prediction (1–3). In fact, the studies have shown evidence of harm—increased CHD events in the first year of treatment and increased stroke and venous thromboembolic events. Although these trials have acknowledged limitations, including use of only a single hormone preparation and participation of older women after many hormone-free years (a practice not usually followed in clinical care), the consistency of these results clearly does not support the use of postmenopausal hormones for prevention or treatment of CHD in women (4).

This leaves us with a growing population of middle-aged and elderly women who have lost the cardiovascular protection of their younger years and for whom unique sex-specific preventive and treatment strategies do not exist. Assessing risk and using effective preventive strategies in these women is critical: CHD is by far the leading cause of death, and deaths due to cardiovascular disease are increasing in American women despite advances in prevention and therapy (5). Women have higher mortality rates and are less likely to receive standard interventions after myocardial infarction than men (6). The prevalence of obesity and type 2 diabetes is increasing, particularly among African-American women, which also increases CHD risk (7, 8). Historical improvements in smoking prevention and cessation, dyslipidemia treatment, and hypertension control have stagnated, further adding to the problem (9). Risk factors for CHD events in persons with established CHD have largely been defined in men, leaving providers with an inadequate body of evidence on which to base secondary prevention of CHD in women.

The Heart and Estrogen/progestin Replacement Study (HERS) collected extensive data on CHD risk factors and medication use, as well as CHD outcomes in 2763 older postmenopausal women (average age, 67 years) with established CHD. These women were randomly assigned to combined conjugated estrogen plus progestin versus placebo and followed for an average of 4.1 years (1, 2). In this issue, Vittinghoff and colleagues (10) analyze data from this study to identify risk factors for myocardial infarction and CHD death and describe use of secondary prevention strategies by the participants. Using 11 variables that were significant from unadjusted models, they calculated hazard ratios with multivariable Cox proportional hazards models.

The strongest predictor (hazard ratio, 1.79 [95% CI, 1.27 to 1.62]) of subsequent events was the presence of many previous myocardial infarctions. Other robust (hazard ratio $\geq$ 1.5) risk factors included evidence of established vascular disease in the form of renal dysfunction (creatinine clearance $<$ 40 mL/min), treated diabetes (receipt of insulin or oral hypoglycemic agents), and angina. Evidence (history or symptoms) of congestive heart failure and African-American ethnicity were also associated with increased risk for CHD events. Of interest, uncontrolled hypertension (systolic blood pressure $\geq$ 140 mm Hg or diastolic blood pressure $\geq$ 90 mm Hg) was the only "traditional" Framingham risk factor with high predictive value for CHD events; age and smoking were not associated with CHD events and low- and high-density lipoprotein cholesterol levels were only weakly associated (11). Controlled hypertension (history of hypertension with normal blood pressure) was not associated with increased risk, reaffirming the effectiveness of antihypertensive treatment in preventing CHD events in high-risk persons. Elevated lipoprotein(a) levels emerged as a novel risk factor only in the placebo group, since hormone replacement therapy is known to reduce lipoprotein(a) levels (12). The rate of coronary events ranged nearly sixfold, from 1.3% per year for women with no risk factors (except known CHD) to 8.7% per year for those with five or more risk factors.

Several limitations of HERS may have affected the risk assessment of the participants. Participation was voluntary, and exclusion criteria eliminated persons with unstable disease, thus leading to lower event rates and possible underestimates of risk. The age range of participants was narrow (mean [$\pm$SD], 67 $\pm$ 7 years), thus eliminating age as a risk factor. The small sample size of some subgroups (for example, only 13% were current smokers) limited the power to detect potentially meaningful differences. Concomitant treatment with lipid-lowering agents (53% at baseline and 66% at the end of the study) undoubtedly attenuated the predictive value of lipid measurements. The study did not include diagnostic tests, such as electrocardiography, echocardiography, and exercise testing, that would be used in practice to predict CHD outcomes in high-risk women. Finally, the statistical analysis of risk was not a prospectively designed element of HERS. As has been discussed, the post hoc data-driven design increases the probability that biologically meaningless associations will be revealed by chance (13). Despite these limitations, the analysis provides useful guidance for secondary prevention strategies in this understudied population.

The most striking aspect of Vittinghoff and colleagues' analysis was the alarming underuse of proven therapies for secondary prevention of cardiovascular disease. Despite clear indications for these therapies, few HERS participants received β-blockers (33% at baseline and 28% at the end

use of the system by its former and current mayors. Benefits have accrued to the CHC, the hospital, and, most important, the patients, with an improved continuum of care. Such integration of all components of the public health care system is critical to the survival of the safety net in this changing and complicated health care environment. In fact, integration has occurred in other safety net systems, such as Parkland in Dallas, Texas; Cook County in Chicago, Illinois; and Cambridge in Cambridge, Massachusetts.

Acknowledgments: The authors thank the Office of Data Evaluation, Analysis, and Research of the Bureau of Primary Health Care and the National Association of Public Hospitals and Health Systems for the data they provided for this research.

Requests for Single Reprints: Patricia Gabow, MD, Denver Health, 660 Bannock Street, MC 0278, Denver, CO 80204; e-mail, PGabow@dhha.org.

Current author addresses are available at www.annals.org.

References

1. **Blaisdell FW.** Development of the city-county (public) hospital. Arch Surg. 1994;129:760-4. [PMID: 8024459]

2. National Association of Public Hospitals and Health Systems 1997 Annual Survey. Washington, DC: National Association of Public Hospitals and Health Systems; 1997.

3. Office of Data Evaluation, Analysis, and Research. Bureau of Primary Health Care 1998 Uniform Data System. Bethesda, MD: Bureau of Primary Health Care; 1998.

4. **Geiger HJ.** Community-oriented primary care: the legacy of Sidney Kark [Editorial]. Am J Public Health. 1993;83:946-7. [PMID: 8328614]

5. **Hollister RM, Kramer BM, Bellin SS, eds.** Neighborhood Health Centers: What Do Demonstration Projects Demonstrate? Lexington, MA: Lexington Books; 1974.

6. **Sardell A.** The U.S. Experiment in Social Medicine: The Community Health Center Program 1965-1986. Pittsburgh, PA: Univ of Pittsburgh Pr; 1988.

7. National Association of Public Hospitals and Health Systems. America's Safety Net Hospitals and Health Systems: Their Situation at the End of the Millennium, What Americans Think, What Policymakers Must Do. Washington, DC: National Association of Public Hospitals and Health Systems; 1999.

8. National Association of Public Hospitals and Health Systems. The Safety Net in Transition: Increasing Your Role in State Design of Medicaid Managed Care Programs, Monograph I. Washington, DC: National Association of Public Hospitals and Health Systems; 1996.

9. Public Health Service Act, §329(f)(3)(G), §330 (e)(3)(G), USC42.

10. BBC Research and Consulting. Denver Community Health Services Family Health Centers: An Analysis of Patients and Communities Served. Prepared for: Denver Health; 1999.

11. **Singer JD, Davidson SM, Graham S, Davidson HS.** Physician retention in community and migrant health centers: who stays and for how long? Med Care. 1998;36:1198-213. [PMID: 9708592]

12. Colorado Community Health Network. Salary and Benefits Survey of Colorado Health Centers. Denver, CO: Colorado Community Health Network; 1999.

of the study) or angiotensin-converting enzyme inhibitors (18% at baseline and 28% at the end of the study), whereas more were given lipid-lowering agents (66% at the end of the study) and aspirin or other antiplatelet agents (83% at baseline and 79% at the end of the study). Paradoxically, women with more risk factors (≥5), and hence more potential benefit, were less likely than those with no risk factors to receive aspirin or other antiplatelet drugs (76% vs. 85%, respectively) or lipid-lowering therapy (59% vs. 72%, respectively) at the end of the study. This report confirms previous evidence that women with CHD are being undertreated in the United States (6).

Although HERS did not show cardioprotective effects of hormone replacement therapy in postmenopausal women, it did highlight a terrible discrepancy between what we know and how we treat our sisters and mothers. Current guidelines for secondary prevention of atherosclerotic cardiovascular disease include use of pharmacologic treatments to prespecified goals (blood pressure < 140/90 mm Hg, or lower if comorbid conditions are present; low-density lipoprotein cholesterol level < 100 mg/dL), as well as lifestyle modification for smoking cessation, regular physical activity, and weight and diabetes management (14). Evidence from randomized, controlled trials indicates that these interventions are effective in preventing CHD events in high-risk women (15–17). Furthermore, experience in the HERS cohort supports this conclusion: Rates of nonfatal myocardial infarction, CHD death, total mortality, and venous thromboembolic events were lower among statin users (18). In addition, recent evidence shows that lifestyle modification can prevent type 2 diabetes (19), reduce blood pressure or prevent clinical hypertension (20), and improve lipid profiles, thus reducing CHD risk and the need for aggressive pharmacologic therapies. Proven tools to prevent CHD events in women exist. A call to action is needed to implement them.

Andrew P. Miller, MD
Suzanne Oparil, MD
The University of Alabama at Birmingham
Birmingham, AL 35294-0007

Requests for Single Reprints: Suzanne Oparil, MD, The University of Alabama at Birmingham, 1034 Zeigler Research Building, 703 19th Street South, Birmingham, AL 35294-0007; e-mail, soparil@uab.edu.

Current author addresses are available at www.annals.org.

Ann Intern Med. 2002;138:150-151.

References

1. Hulley S, Grady D, Bush T, Furberg C, Herrington D, Riggs B, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group. JAMA. 1998;280:605-13. [PMID: 9718051]

2. Grady D, Herrington D, Bittner V, Blumenthal R, Davidson M, Hlatky M, et al. Cardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/progestin Replacement Study follow-up (HERS II). JAMA. 2002;288:49-57. [PMID: 12090862]

3. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. JAMA. 2002;288:321-33. [PMID: 12117397]

4. Mosca L, Collins P, Herrington DM, Mendelson ME, Pasternak RC, Robertson RM, et al. Hormone replacement therapy and cardiovascular disease: a statement for healthcare professionals from the American Heart Association. Circulation. 2001;104:499-503. [PMID: 11468217]

5. 2002 Heart and Stroke Statistical Update. Dallas: American Heart Assoc; 2001.

6. Vaccarino V, Parsons L, Every NR, Barron HV, Krumholz HM. Sex-based differences in early mortality after myocardial infarction. National Registry of Myocardial Infarction 2 Participants. N Engl J Med. 1999;341:217-25. [PMID: 10413733]

7. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999-2000. JAMA. 2002:288:1723-7. [PMID: 12365955]

8. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care. 1998;21:518-24. [PMID: 9571335]

9. Cooper R, Cutler J, Desvigne-Nickens P, Fortmann SP, Friedman L, Havlik R, et al. Trends and disparities in coronary heart disease, stroke, and other cardiovascular diseases in the United States: findings of the National Conference on Cardiovascular Disease Prevention. Circulation. 2000;102:3137-47. [PMID: 11120707]

10. Vittinghoff E, Shlipak MG, Varosy PD, Furberg CD, Ireland CC, Khan SS, et al. Risk factors and secondary prevention in women with heart disease: the Heart and Estrogen/progestin Replacement Study. Ann Intern Med. 2003;138: 81-9.

11. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation. 1998;97:1837-47. [PMID: 9603539]

12. Estelles A, Cano A, Falco, Espana F, Gilabrt J, Grancha S, et al. Lipoprotein(a) levels and isoforms and fibrinolytic activity in postmenopause—influence of hormone replacement therapy. Thromb Haemost. 1999;81:104-10. [PMID: 10348700]

13. Furberg CD, Vittinghoff E, Davidson M, Herrington DM, Simon JA, Wenger NK, et al. Subgroup interactions in the Heart and Estrogen/progestin Replacement Study: lessons learned. Circulation. 2002;105: 917-22. [PMID: 11864918]

14. Smith SC Jr, Blair SN, Bonow RO, Brass LM, Cerqueria MD, Dracup K, et al. AHA/ACC Guidelines for Preventing Heart Attack and Death in Patients With Atherosclerotic Cardiovascular Disease: 2001 update. A statement for healthcare professionals from the American Heart Association and the American College of Cardiology. J Am Coll Cardiol. 2001;38:1581-3. [PMID: 11691544]

15. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet. 1994;344: 1383-9. [PMID: 7968073]

16. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomized placebo-controlled trial. Lancet. 2002;360:7-22. [PMID: 12114036]

17. Lonn E, Roccaforte R, Yi Q, Dagenais G, Sleight P, Bosch J, et al. Effect of long-term therapy with ramipril in high-risk women. J Am Coll Cardiol. 2002; 40:693-702. [PMID: 12204499]

18. Herrington DM, Vittinghoff E, Lin F, Fong J, Harris F, Hunninghake D, et al. Statin therapy, cardiovascular events, and total mortality in the Heart and Estrogen/progestin Replacement Study (HERS). Circulation. 2002;105:2962-7. [PMID: 12081988]

19. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393-403. [PMID: 11832527]

20. Whelton PK, He J, Appel LJ, Cutler JA, Havas S, Kotchen TA, et al. Primary prevention of hypertension: clinical and public health advisory from The National High Blood Pressure Education Program. JAMA. 2002; 288:1882-8. [PMID: 12377087]

© 2003 American College of Physicians–American Society of Internal Medicine